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The American Heart Journal

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The American Heart Journal

VOL. VI JUNE, 1931 No. 5

Original Communications

THE CORONARY ARTERY IN HEALTH AND DISEASE*

JAMES B. HERRICK, M.D.
CHICAGO, ILL.

THE title of this paper is a misnomer. It is too pretentious. He would be bold indeed who would presume to present in a single lecture all the facts connected with the coronary artery, and the solution of its numerous problems that have immediate or remote contacts with moot and recondite questions of anatomy, pathology, physics, chemistry, physiology. And it would be rashness itself if the attempt were made by one whose training has been chiefly along clinical lines. For the sake of one's reputation also, it is wiser to keep silent regarding some of these topics. Chaucer in his translation of Boethius' *Consolations of Philosophy*—the idea is Boethius' really, and not Chaucer's—has this delicious bit: "This feynede philosophre . . . seyde at the laste right thus: 'understondest thou not that I am a philosophre?' That other man answerde again ful bytingly, and seyde: 'I hedde well understonden it, yif thou haddest holden thy tonge stille.'" There is a lesson here that I have tried to take to heart. Often in the writing of this paper—perhaps not often enough—it has kept me mute when I have been tempted to speak. The caption might better be: "Comments on the Coronary Artery and Its Diseases from the Clinical Point of View."

In the last thirty or thirty-five years there has been a revival of interest in, and a revision of our ideas of, the heart and its diseases. This is the period of the polygraph, the electrocardiograph, heart-block, circus movements, bacterial endocarditis, Aschoff bodies, quinidine.

In this re-study of the heart, the coronary artery naturally has had attention. But it is only in the last twenty years and particularly in the last decade that the interest in the normal and pathological anatomy, the physiology and diseases of this important vessel has become keen and widespread. In this paper the approach to the subject will be by way of clinical medicine. That was my avenue of approach about twenty

*The Harvey Lecture, read at the New York Academy of Medicine, March 19, 1931.

years ago when my attention was sharply attracted to the subject by a case of acute thrombosis of the coronary artery. It is chiefly by a consideration of the clinical and pathological features of acute occlusion of the artery that American physicians became interested in the subject and made so many noteworthy pioneer observations.

The acute or subacute type with frank symptoms is the one that is best known; it is the form that is generally meant when coronary occlusion or infarct of the myocardium is mentioned. In the United States it is regarded as not uncommon. Yet many writers, especially in Europe where a comparatively tardy interest has been manifested, still refer to it as rare. It is plain that what we look upon as acute infarction either is not so common in Europe as in this country or is classed as some other affection, perhaps angina pectoris. When one recalls one's own experience or talks with colleagues concerning theirs; when one reads the reports of cases by Levine, Conner and Holt, Willius, and Barnes, each with a series close to, or above, the hundred mark; when one learns that the Medical Department of one of the large life insurance companies in 1930 had 239 death claims in which the attending physicians returned diagnoses of coronary obstruction; when one considers the many cases of sudden death caused by acute thrombosis, cases that more often come to the attention of the coroner than of the practitioner; and when one includes also the often unrecognized mild and latent cases, one is convinced that the condition is not a rarity. We may add that coronary thrombosis is seen not alone in North America and Europe. Reports come from other continents. Last year Battro of Buenos Aires published an excellent monograph with clinical and experimental observations.

The question naturally arises whether the remarkable prevalence is due to an increasing frequency of coronary thrombosis or is merely due to the fact that the condition is better recognized today than formerly.

If we review the older literature; if we re-read Osler, Huchard or Mackenzie in the light of present-day knowledge, we see that not a few cases regarded as angina were evidently cases of infarction. And the splendid monographs of René Marie on infarct of the myocardium (1897) and of Sternberg on partial aneurysm of the heart (1914) are teeming with records, the clinical significance of which was overlooked because the vision of the writers as of the readers was focussed on the pathology. It is clear that this is no new disease.

It may seem incredible that such startlingly dramatic symptoms should so long escape the attention of physicians and pathologists. Yet strange, almost ludicrous, oversights are no novelty in medical history. Typhus and typhoid fevers were long confused. The development of a clear cut conception of appendicitis is well within the memory of many of us. For how long a time have undulant fever, encephalitis, tularemia and other supposedly rare diseases been given a wrong or meaningless

label? One of the explanations then, probably the chief explanation, for this apparent increase is a better understanding and more frequent recognition.

On the other hand, there is an impression, supported by several studies, that thrombosis in general is on the increase. While reference is chiefly to thrombosis in veins, it may be that the same causes, whatever they are, operate to multiply the instances of arterial thrombosis, especially in the coronary arteries.

The explanation offered by some that the development of thrombi is favored by the more frequent use of drugs intravenously does not seem attractive, at least in regard to arterial thrombi. I am certain that in only a very small proportion of my patients has there been previous intravenous therapy of any kind—arsphenamin, vaccines or what not. Nor do Singer's studies from the Leipzig clinic bear out this theory as to venous thrombosis.

Do modern conditions of living make for an increase? One is tempted to answer that this may be a contributing factor, at least if one believes that the strenuous life with its speed mania tends to cause hypertensive and arteriosclerotic states, of which general conditions the coronary lesion is often but a part. It is also true that today more people are reaching adult or senescent years when degenerative vascular changes come on. Therefore, there are more coronaries to be affected with the lesions that favor thrombosis.

Does infection play a leading part in producing thrombosis in the coronaries? We are told that recent infections may cause an acute arteritis or a former infection may perhaps sensitize the vessel wall. In either case, it is suggested, thrombosis may be favored. Are some of the cases we are encountering today of the crop that was sown by the influenza pandemic of 1918? Why is thrombosis rare in rheumatic hearts though rheumatic mural changes in the vessels are not unknown, perhaps not unusual? Why does syphilis spare the main coronary trunks? What about Warthin's idea that syphilis, while not an immediate cause of coronary thrombosis, is a secondary influence in predisposing to such thrombosis as well as in causing sudden death? What of thrombosis in the veins of the heart? Are the veins as carefully observed as they should be, by the pathologists? The relation of infection to coronary thrombus formation is still an open question. The problem needs further study.

The essential lesion seems to be a narrowing of the vessel due to disease of the arterial wall that is generally rough from calcification. Marie said that coronary thrombosis always is due to a disease of the artery. "It is never spontaneous." Yet other factors may enter: The sluggishness of the blood current; qualitative and quantitative physical and chemical changes in the blood; variations in its viscosity or its content of albumin; alterations in the number of platelets or their

fragility. Whether changes in food, in the air we breathe, especially in our large cities with their automobile and factory fumes, may have an influence, is a matter for surmise. So far, no definite facts along this line are known.

The question is sometimes asked, why are the coronary arteries oftener the seat of arteriosclerosis and thrombosis than other arteries in the body. In answer, it is said that circulatory conditions in the heart are unique. The ceaseless motion of the coronaries, their constant subjection to extreme active and passive stress and pressure, their unusual kinks and tortuosities may help to explain a striking development of sclerosis with consequent thrombosis. Yet it is not clear why an artery that is almost never quiet should so readily develop thrombi.

Moreover, are the coronaries oftener involved in thrombosis than other arteries of similar size? The startling phenomena that so commonly announce the formation of coronary thrombi, together with the serious effects that follow, make them stand out as star performers in the tragedy of vascular disease that is always on the boards. Do figures show that the vessels of the brain, spleen, kidney, pancreas are less often thrombotically closed than those of the heart?

Acute obstruction has bulked large in the consideration of coronary disease. The earlier drawn clinical picture with its severe enduring, substernal or epigastric pain, unprovoked by effort, its attendant shock, lowered blood pressure, disordered and weakened heart condition, dyspnea, fever, leucocytosis, pericardial rub, embolic complications; with death in a few hours or days from ventricular fibrillation or rupture, or with partial or complete recovery after a slow convalescence, this still stands as our type.

One often hesitates on the basis of slight active and residual manifestations to diagnose a condition traditionally and in reality so formidable. We must, however, admit into the cadre of the acute and subacute cases many milder and atypical types in which supposedly cardinal symptoms may be lacking.

Without taking up the details of these atypical forms—they are discussed by various authors—it may not be amiss to make a brief reference to the painless cases. Acute coronary obstruction has so naturally and unconsciously been associated in our minds with angina pectoris in which pain is almost by definition a part of the symptom complex, that it is difficult to eliminate this feature from our clinical conception of the accident. Yet it is clearly established that painless acute obstruction occurs.

It has been suggested, that normally certain areas of the heart are not only less vital than others, indifferent or silent they have been called, but also less sensitive. At autopsy fresh infarcts are sometimes found associated with multiple areas of fibrosis that speak for previous obstruction of small branches, yet no pain has been noted, no pain even

announcing the recent infarction. There has evidently been a very gradual and progressive narrowing of the artery by sclerotic processes. The area irrigated by the artery has become relatively inactive, relatively anesthetized by destruction of vessels, nerves and functioning muscles, so that a painful response to the new obstruction is lacking. The final complete obstruction comes without a sudden shock, the element of surprise is lacking as the heart is in a sense prepared for the supreme insult. Abrupt heart failure with its dyspnea and other phenomena may be present, but pain may be lacking. These are the "substitution symptoms" in the hyposensitive described by Libman. As Obratzow and Straschesko expressed it, dyspnea may be the pain equivalent.

There is every clinical gradation in the severity of symptoms resulting from the sudden obstruction of the coronary artery, severe, moderately severe, mild. As results, early death, often sudden death, death after a cardiac breakdown, or a partial recovery with myocardial weakness as a hang-over, or perhaps a complete symptomatic restoration of function. These varying manifestations as well as the varying results must depend in large measure on the size, location, and functional importance of the arteries and muscular areas involved. They depend also on the degree to which compensatory enlargement of anastomosing vessels has prepared the heart for the attack.

Clinical features will depend to a large extent on the rapidity with which the obstruction is accomplished. The element of time is of great importance. American physicians and experimenters, heretofore largely concerned with the acuter cases, must consider as well the group that may be called chronic. As this group is approached, it is realized that there is a difficult task ahead. To clear away the vagueness surrounding "chronic myocarditis," to differentiate at the bedside and in the dead-house between a process that in the stricter sense is inflammatory and one that is degenerative, the end-result of obstructive lesions, to learn what heart disturbances, especially what cases of heart failure, are due to slowly progressive coronary disease is a big undertaking. In the chronic cases there may be no dramatic announcement of the climax of the myocardial tragedy by sudden pain, dyspnea or drop in pressure. Often there is an insidious, gradual breakdown of the heart's efficiency with easily provoked dyspnea and palpitation together with irregularities and edema, due to the slow development of multiple areas of fibrosis that may by confluence become of considerable size. To quote Gallavardin's graphic and epigrammatic statement, the large infarcts are often infarcts that have enlarged, i.e., have grown to be large. "Les grandes infarctus sont souvent des infarctus qui ont grandi." By this is not meant that all cases formerly called heart failure, chronic muscular insufficiency, dilatation of the heart, or break in compensation, are to be regarded as due solely to slowly developing obstruction in the

coronary arteries. Not at all. There are cases of heart failure due to rheumatic carditis in which with distinct valvular and myocardial lesions the arteries are comparatively healthy. Syphilis may be a cause even when the main arterial trunks are normal. The heart in obesity, in wasting diseases, in anemias; the worn-out heart associated with chronic nephritis, emphysema, scoliosis, goiter, may show no significant lesions in the coronaries. And there are cases in which intoxication and a vague something spoken of as fatigue are called in to explain the giving out of a heart that anatomically seems still fit to function. But the number of cases of heart failure due to progressive obstructive coronary lesions is very large. The coronary artery is a prolific disturber of health.

It is often difficult, at times impossible, to recognize these diseases, clinically. Morawitz laments the fact that the physician is so often chagrined because the autopsy discloses coronary conditions so different from what had been predicted. R. Kaufmann recently said that the pathologist looking at two hearts similarly involved in coronary sclerosis with secondary myocardial fibrosis, cannot tell in which case there has been a stormy clinical upset and in which case the symptoms have been mild and latent. We may well employ the term freakish, as does Ceelen, to describe the entire arteriosclerotic process as well as its clinical manifestations.

Without elaborating this topic one may say in a general way that when a failing heart other than the heart of rheumatism or syphilis gives out more rapidly than is the rule, when cardiac asthma and acute pulmonary edema precede or accompany a drop in a previously high blood pressure, when gallop rhythm, feebler and more diffuse apex impulse with systolic mitral murmur appear and when in spite of rest and digitalis the heart fails to come back, there has perhaps, or probably, been an occlusion of a coronary artery or some of its branches with resulting infarction. This event—an epiphenomenon, Gallavardin aptly calls it—hurries the heart to its breakdown to which it was already slowly but surely progressing.

I wish to insert a comment concerning the diagnostic value of vagus pressure in suspected coronary disease. Wenckebach in 1914 in his book on the "Irregularities of the Heart" stated that a marked slowing of the heart produced by pressure over the carotids in the neck, especially the right carotid, was an evidence of myocardial weakness. Several writers, few in this country, have written on this subject. Opinions differ as to the worth of the test. My own impression is that there is something to it. Its almost uniform absence in those whose coronaries and heart muscle are presumably healthy—the young and cardioneurotic individuals; its increasing frequency in the senescent, aged and arteriosclerotic; the sometimes startling cessation of the heart beat in patients whose coronaries have recently been occluded and in

those whose hearts are inefficient, supposedly from myofibrosis, have made me feel that the test is of some value. One must agree, however, that Wenckebach is right in not assigning to it the virtues of an infallible sign; it may be lacking when one would expect it, it may be manifest at least to a moderate degree when one sees no reason for its presence. It may be added that the results of this simple pressure over the carotid are not alone confined to slowing of the heart's rate. There are, as was shown several years ago, in one of the most important contributions concerning the subject, being that of your presiding officer, Alfred Cohn, differences between the effects of stimulating the right and left vagus. The former has an influence that is especially chronotropic, the latter dromotropic. Other results shown chiefly through the electrocardiogram and of especial physiological interest, need not concern us here. The test needs further study at the bedside as well as in the laboratory. Even the rationale of its production is not yet agreed upon. Hering, it will be recalled, does not accept the direct vagal stimulation explanation. He regards it as a carotid sinus reflex.

In the study of coronary disease much use has been made of electrocardiography. Without attempting a comprehensive review of this topic, I wish to call attention to a few facts that seem to warrant consideration.

Taking up first the electrocardiogram in acute obstruction; when local necrosis of the myocardium has been brought about acutely by direct experimental destructive injury of tissue, or in an indirect manner by cutting off the coronary circulation as by ligation; or when such myomalacic lesion in man is the result of coronary thrombosis or the rare surgical ligation of the artery for stab wounds, fairly characteristic electrocardiographic findings have been noted. One feature needs repetition lest it be forgotten. It is that the electrocardiogram in these cases of acute myocardial destruction is not fixed, that for a long time it undergoes change. This was shown experimentally even as far back as 1910 when Eppinger and Rothberger injected silver nitrate into given areas of the heart muscle. It was observed by Samajloff in 1911. Fred Smith, in his classic experiments, showed that after ligation of the left coronary artery of dogs, especially the descending branch, fairly uniform changes were noted in the electrocardiogram, a prompt increase in the height of the T-wave, with a subsequent early drop to a negative state and then a slow return toward, or to, its old positive position. Smith's work on the coronaries of dogs has been quite generally confirmed as has the transference of most of these results to man. There are numerous clinical observations confirming this feature of the experiments. The very title of Parkinson and Bedford's article, "Successive Changes in the Electrocardiogram After Cardiac Infarction (Coronary Thrombosis)," declares that the picture is not fixed. But not all writers, and by no means all practitioners, take account of the

fact that the electrocardiogram, registering regressive and reparative processes should and does show variations from day to day or month to month. The physician who gets his tracing right after the accident sees the prominent T-wave with the high take-off from R-wave. The one whose tracing is made a week or several weeks later stresses the altered, often inverted, T-wave or the Pardee coronary wave or some peculiarity of QRS, perhaps its broadening or slurring. Each observer is apt to generalize and declare that such and such a picture is characteristic—*the* characteristic it is sometimes expressed—of acute coronary obstruction. Conflicting and confusing statements might be avoided if the time relations were better realized, if it were recognized that the pathological process is for many weeks at least, one of change, which change is reflected in an electrocardiogram that for a long time is not stable.

A second point: Not all the electrocardiographic abnormalities noted in a given case are necessarily due to some recent event heralded by symptoms suggestive of acute coronary or myocardial accident. The *post hoc ergo propter hoc* argument is as fallacious here as in therapeutics. Earlier gradual narrowing and blocking of diseased vessels may have resulted in myocardial fibrosis, the process being as varied and as scattered as to time as the lesions are as to size and location. The electrocardiogram, translating the progressive myocardial changes, may be evolutive as Clerc has called it, complexes broaden and flatten, extrasystoles appear or auricular fibrillation with paroxysms of tachycardia and perhaps final "anarchy." Some of the abnormal, bizarre tracings then, may be due to old lesions long antedating the present symptoms, or may be associated with cardiac hypertrophy attendant on hypertension. Carter in the discussion last year in the Association of American Physicians very justly emphasized these points.

But aside from these considerations there is need for still further study of electrocardiography in acute and chronic cases.

There is a consensus of opinion that changes in the T-wave are the ones most frequently seen in a recent or old coronary obstruction; Nathanson says in 88 per cent of cases. Inversions in Leads I or II, the "high take-off," Pardee's coronary wave are met with so often that they cannot be regarded as meaningless or accidental. Other changes noted in acute cases, extrasystoles, atrioventricular block, paroxyms of tachycardia of various types, even short paroxysms of ventricular tachycardia, are not so generally regarded as pathognomonic.

But the significance of many alterations seen long after an acute occlusion or when the occlusion has been insidious or slow is not always clear—broad P-waves, a prolonged P-R interval, a QRS complex slightly slurred or perhaps distorted almost beyond recognition by exaggerated notching, broadening and displacement below the line. Even though symptomatically a heart may seem functionally normal, if it records such abnormal electrocardiograms there is reason to believe there

are organic changes that cause interference, not necessarily serious, with conductivity and presumably with other functions as well. But knowledge sufficiently precise to enable one to state definitely what is the location, size or age of the lesion is often lacking. There is no agreement as to the meaning of arborization block. That it has an important significance seems certain. F. N. Wilson and his associates, the Oppenheimers, and others are massing evidence to show that what has long passed for right bundle-branch block is really left branch block and vice versa. Barnes and Whitten on the basis of anatomical, clinical and post-mortem studies, declare that obstruction of the right coronary is more common than generally supposed; that infarcts in the basal posterior portions of the left ventricle and of the septum and at times even of the apex may be produced by such obstruction. They believe that by a study of the electrocardiogram, grouping the tracings after the classification of Parkinson and Bedford, one may with some approach to accuracy know whether the obstructing clot is in the right or left coronary. Their suggestive work should be confirmed. They and others raise the important question as to how far human electrocardiograms may be compared with those obtained experimentally in the dog, for there are anatomical differences. Some of the posterior wall of the left ventricle, and parts of the septum that in the dog are generally nourished by the left coronary are cared for in man by the right. In this connection the recent work of Moore, Campbell, Gross, and Whitten is important.

What of a lowering of the various peaks, the so-called low voltage tracing? Does this mean merely a general weakening of the myocardium? Reappearance of higher voltage tracings after rest would seem to speak for such an interpretation in some instances. Or has the low voltage curve a more restricted significance? H. J. Stewart asks whether it may not mean a shutting off of the left circumflex artery as suggested by Fred Smith's experimental work as well as by a few clinical cases with autopsy control that have been reported. What of an exaggerated Q-wave in Lead III? It is more and more persistently, and it would appear justifiably, clamoring for admission into the select company of "high take-offs," inverted T's, and convex RT's that claim title to the coronary-crowned-peerage because they came in with William of Holland—William Einthoven—when he invaded and conquered the realm of cardiology. There is food for thought in Craib's conclusion that "the alteration in the electrocardiogram that results from local myocardial infarction depends upon the normal contribution of the region in question. . . . When 'silent areas' are infarcted the electrocardiogram is unaltered provided the infarction is not accompanied by gross dilatation or conspicuously diminished output per beat."

It is evident that there is need for further investigation of electrocardiography as related to coronary disease. Much as it goes against

the grain to admit our poverty of knowledge on this point, one must agree with Gilbert and Ritchie when, as the conclusion of their most critical study and summary of electrocardiography in myocardial infarctions and fibrosis, they say: "The evidence available at the present time does not lend support to the view that the form of the electrocardiographic distortion can be regarded as a definite localization of the infarct." Reports based on the study of large series of cases may carry conviction by the sheer weight of numbers, but critical reports of carefully worked out single cases, such as that of H. J. Stewart two years ago, also deserve commendation; the conclusions may be as convincing as those drawn from the larger series.

There is especial need of a study of the electrocardiogram in cases of coronary sclerosis of a chronic character, cases of disseminated myocardial fibrosis, of angina pectoris, of chronic myocarditis *sensu strictiori* such as may have resulted from rheumatic, syphilitic or other infectious processes. Besides, the transitory deviations from the normal electrocardiogram seen in acute infections as rheumatism, diphtheria and influenza, in uremia, in digitalization, etc., need further investigation.

It is important that clinical reports should describe more accurately the location of pain, its radiation, its deviation, skin tenderness; location of pericardial friction; degree of cyanosis, pulmonary and hepatic congestion; height of temperature; number of leucocytes; change in blood pressure. There are reasons why pain radiates to the epigastrium in one case, to the right arm in another, to the left arm in a third; why in one case there is a temperature of 102 degrees, in another that seems to be equally severe no fever at all; but the reasons are as yet obscure. By such careful bedside observation together with electrocardiograms taken at short intervals, and when possible with post-mortem examinations that take account of minute anatomical changes, much can be learned as to the nature and localization of these coronary lesions. New light may be shed on the physiology and pathology of the heart that may have rich application in practice. Gilbert and Ritchie state that up to 1930 there are only 148 case reports with sufficient detail to permit of satisfactory analysis. In only forty-four of these cases are post-mortem records available. I have elsewhere said, some cardiac Beaumont may yet find his Alexis St. Martin so that clinical, including electrocardiographic, data, may be based on observations made on man with conditions largely under experimental control.

It is desirable that our knowledge should be clarified and that as soon as possible. The electrocardiograph is more and more used in hospitals and in private practice. But it is here and there falling into disrepute. We often see the tracing interpreted by physicians of no special training, even by technicians who are not physicians at all. The assurance with which some of these pathological and topographical diagnoses are made is rather startling to one who is at all familiar with the surprises

of the dead-house. Minute, almost microscopic slurrings, slightest variations from the classic electrocardiogram are confidently declared to indicate some particular coronary or myocardial lesion, at times with a prognostic warning that all too often upsets the mental equilibrium of the practitioner, still more that of the patient. And these cocksure interpretations, as shown by subsequent events, are often wrong. All this may ultimately lead to a distrust of the electrocardiograph as an instrument that is even approximately precise. Such distrust is already manifest. "There was no negative T-wave, no coronary wave yet an infarct was found," or "a negative T was present and a broad QRS and yet no lesion was discovered, etc. What can we believe?" Some of the hospital and commercial laboratories recognizing this lack of definite knowledge, have become very wary and shrewd, perhaps we should say wise. They send in diagnoses of "myocardial damage." Possibly what is lost in definiteness of diagnosis is made up in a closer approximation to truth. Of course, the electrocardiograph is not at fault. It is our knowledge that is faulty.

When I began this paper I fully intended to discuss—I will not say settle—the question of the origin and nature of pain in angina pectoris. I have given up this plan. After reading many articles I found that my own notions, none too clear to start with, were still very nebulous, even more nebulous. I feared my presentation of the subject would not be convincing, for it is difficult to convert another to views that one is not certain about oneself. Besides, while there are many excellent discussions of the subject, many are but specious pleadings for the writer's pet theories, exercises in dialectic with little or no scientific proof. At times in reading the fine-spun academic and wordy arguments, one is reminded of the momentous question as to the proper way to open the egg and the heated controversy that arose therefrom between the Big-Endians and the Little-Endians, for details of which one may consult the immortal Lemuel Gulliver. Much of the recent discussion centers about experimental and surgical investigation concerned with the cervical sympathetic nerves and ganglia. As someone has said this work is based on an anatomy that is not precise, and a physiology that is poorly understood. While thus embarrassed by my own ignorance and by the bewildering conflict of views contained in the staggering mass of literature, I ran across several frank statements that comforted me and strengthened me in my decision to omit this feature. This by Wiggers: "An intelligent discussion of cardiac pain is not at present possible, for ideas as to the ultimate mechanisms producing pain remain wholly speculative." And one by Clerc who, referring to the origin of angina pectoris as still a mystery, says that in the future as in the past, pages will be devoted to this enigma, and as another has stated, the course already pursued is short compared to that which must be followed before the goal is reached. And a third from Italy: "Angina pectoris

is an illness syndrome. Its pathogenesis is obscure; the etiological facts are uncertain and incomplete; the data of anatomical pathology, experimental physiology and physiopathology are insecure and bristling with inexplicable contradictions." If such are the views of a scientist unusually well informed as to cardiovascular physiology, and of physicians well read and with rich laboratory and clinical experience, why should I add to the bulk of this fruitless phraseology? Lapsing into the vernacular, I pass.

I cannot, however, resist the temptation to say a word as to the bearing of acute occlusion on the theories of angina pectoris. A clinician must have some notions on this point, speculative if not conclusive.

At the outset it may be said that in subscribing to the coronary theory of angina one need not deny that a diseased aorta may cause pain, a pain that at times is like that of coronary angina but that often lacks the earmarks of the typical form.

The two theories that have prevailed for two or more decades are the aortic and the coronary. Allbutt and after him, Wenckebach, Rudolf Schmidt, Vaquez, and many others have contended that the pain is due to a stretching of the diseased wall of the aorta. "Entzündung and Dehnung" is the explanation of Schmidt. "For me," declared Allbutt, "the coronary hypotheses are dead and buried." Many physicians, however, still cling to, and increasing numbers of them are becoming adherents of, the coronary artery theory, the theory that with various modifications has been the prevailing one since the time of Parry and Jenner.

Experience with cases of acute thrombosis of the coronary artery seems to strengthen the view that the paroxysm of angina of effort has its origin in a perversion of function of the coronary artery or the muscle supplied by that artery, or of both.

There can be no denial that the sudden closure of a coronary artery or one of its larger branches is often attended by pain that may resemble in every particular that of angina pectoris. Patients who have had previous anginal attacks on walking often speak of it as of the same kind only more severe, more persistent, more prostrating. It is unreasonable to assume that the pain preceding the occlusion has had its seat in the aorta while the similar though severer pain clearly has its origin in the obstructive lesion in the coronary artery. To contend that in the latter case the pain is really of aortic character because the pathway of transmission of the stimuli to the brain is by way of nerves that pass through the aortic adventitia on their way to the sympathetic trunks and the cord, seems illogical. One might as well argue that if the little finger is pinched in the door the pain has its origin in the ulnar nerve in the cubital fossa or in the brachial plexus because the ulnar nerve passes these points on its way to the cord and brain. The origin of the pain

is clearly in the crushed finger in the one case, in the coronary artery or the damaged muscle in the other.

Wenckebach lays stress on the fact that previous anginal pain generally ceases after an extensive infarction. This, he says, speaks for a resulting weakness of the ventricular wall, and a lessened pressure on the aortic wall. In reply one may say that there is no uniform result in regard to pain of an anginal character that follows a thrombotic accident. By no means do all cases of even extensive infarction lose their anginal pain. The status anginosus may continue for hours or days though muscular power is weak and blood pressure low. Not all patients who do lose the pain show lowered blood pressure or ventricular weakness. Furthermore, many patients have their effort angina ushered in by a stormy bout clearly due to obstruction of a coronary artery. May it not be that in some instances anginal pain ceases after the thrombotic occlusion because the artery with its nerves, and the affected patch of myocardium are in effect dead, functionless, incapable of responding to the stimulus of effort that formerly induced pain? May it not be that the fibrous patch has lost nearly all its specific functions like conductivity and contractility and is relatively painless? It may retain little except the rather characterless function of holding, i.e., not breaking. The very fact that when the vessels and the muscle cease to act there is no pain-response on effort speaks strongly for a direct connection between such artery or muscle or both and the pain of angina. When an attack of coronary thrombosis initiates anginal symptoms, may it not be that the artery is not completely shut off, or that some smaller branches are left partially occluded, capable on effort of inducing the condition—let us assume relative myocardial ischemia, anoxemia if you prefer, perhaps associated with spasm—that causes pain? The close association of the symptoms of these two conditions, obstruction in a coronary and pain, is something more than accidental. For the purpose of this argument it is immaterial whether the pain begins or ceases with the coronary occlusion. Either phenomenon is clearly associated with a suddenly developed anatomical change in the coronary artery and not in the aorta.

Take a case like this: A man of forty-seven years, supposedly in good health, is awakened at six in the morning in June, 1930, by a severe substernal pain radiating to both arms, a pain lasting in spite of morphin, for nine hours. He recovers from this attack and goes about his work, feeling quite well until November. Then distress in the sternal region on walking, with pains going to the arms, leads his doctor to diagnose angina, and to put him to bed. Again he improves but about the last of December as he resumes his activity, typical effort angina appears. Walking two blocks, especially in the cold, or after a heavy meal brings on the pain and causes him to stop. The physical examination reveals little that is abnormal. The electrocardiogram,

however, shows in Leads II and III inverted T-waves with the coronary wave of Pardee and some slurring of QRS. Interpreting these facts, there was an acute infarction in June, 1930, with recovery. In November a possible second infarction with less stormy symptoms, then typical angina of effort. Can one reasonably dissociate these phenomena and say that the pain in the first instance was coronary, in the second aortic? Clearly the burden of proof is on him who denies the coronary origin for both pains. This is but clinical evidence, but I see no other reasonable way to interpret the phenomena than on the basis of disturbance in the coronary artery.

There are many other arguments that support the coronary theory against the aortic. I wish to refer briefly to a few of these that have made a special appeal to me.

1. The contention that post-mortem examination generally bears out the aortic theory is not well founded. Not the least valuable part of Hans Kohn's comprehensive survey is his painstaking historical review of original records. He finds that many of the older observers—and some of the later ones are also negligent—really did not examine the coronary arteries or examined them carelessly. The overwhelming number of positive coronary cases would be still further increased if these vessels were examined more thoroughly, not the main trunks alone but smaller branches as well. It is so much easier to find lesions in the large, easily examined aorta than in the smaller coronary! Absence of detectable coronary lesion does not exclude spasm. Presence of diseased coronaries without angina is not conclusive proof of the correctness of the aortic theory. Kohn well says that we must not forget that the anatomical lesion is not the disease, rather the resulting disturbance of function and the reactive changes in the organism.

2. That angina is infrequently found with auricular fibrillation may be true. Auricular fibrillation is most commonly seen in rheumatic hearts, especially with mitral stenosis. But this is exactly where coronary obstructive lesions are rare, viz., in rheumatism.

As a corollary to this argument note the unusual case seen by Coombs and Perry. A child of fourteen with acute rheumatic carditis had angina pectoris, the only instance Coombs had come across in an unusually rich experience with rheumatic children. Autopsy showed marked narrowing of the coronary through acute rheumatic changes in the wall of the artery.

3. There are many hearts of "chronic myocarditis" whose cells are damaged by infectious or toxic processes, e.g., rheumatism, typhoid fever, diphtheria, thyroid toxicosis. Such hearts may give out suddenly or gradually, but only rarely is pain a striking symptom. Only rarely do we find obstructing coronary lesions.

4. With syphilis angina is rare except in cases in which the coronary mouths are narrowed by the aortic process.

5. Nitrites and theobromine compounds dilate the coronaries. They often afford relief in angina of effort. It may be assumed that they relax a spasm or dilate the vessel so that the relative ischemia of the heart muscle is relieved.

6. Levine and others have by the injection of epinephrine provoked painful seizures in patients subject to angina. In younger individuals with supposedly normal coronary arteries no such pain was noted. The explanation offered that the increased work demanded of the myocardium by the rise in blood pressure cannot be met if there are obstructing coronary lesions, seems satisfactory.

7. Hypoglycemia induced by insulin has caused anginal distress. An area of heart muscle already poorly nourished because of arterial narrowing has its nutrition still further cut off by the reduced sugar content of the small amount of impoverished blood.

8. Similarly in severe anemia; blood of poor quality may be insufficient to meet the needs during effort—oxygen needs let us say—of some area in the heart muscle when the quantity of blood is lessened by a partly obstructed coronary; pain may result. In this instance as in hypoglycemia the threshold for pain is lowered by the circulatory insufficiency of the damaged coronary. If the amount of sugar or the amount of oxygen is increased, pain may disappear.

9. In hyperthyroidism whether induced by an inactive gland, or by feeding thyroxine in myxedema, anginal pain may appear. The heart muscle poorly supplied with blood by a damaged artery cannot meet the requirements of increased metabolism. If the metabolic rate be reduced, the angina may disappear.

In the last three instances (7, 8, 9) it is seen that the heart's ability to respond normally and painlessly to an increase in work demanded by exertion, heightened metabolism, greater peripheral resistance, etc., depends as well on the quality as on the quantity of blood that may get through the coronary artery. Means, in an article that has just come to hand, compresses much of this and similar argument into the epigrammatic statement that "the symptom angina pectoris is evidence of relative insufficiency of coronary flow."

10. In patients with angina electrocardiographic changes are frequently seen. As Grotel well remarks, these changes are by no means to be regarded as specific. Yet they are often due to muscular degeneration, the result of coronary disease. This degeneration by its close association with the anginal syndrome surely suggests a more intimate relation to the vessels of the heart proper than to the aorta.

Especially significant are the electrocardiograms taken during attacks of angina. Transitory variations in the ventricular complexes would seem to mean transitory changes in the heart muscle—perhaps coronary spasm and ischemia. Parkinson and Bedford exhibit tracings that resemble those seen at the beginning of coronary infarction. Feil and

Siegel, Bousfield, Willius, Wood and Wolferth and others report altered electrocardiograms during attacks.

11. In a small number of cases vasomotor phenomena, e.g., Raynaud's fingers, have been associated in a suggestive way with angina. Coincident coronary spasm seems far more likely to explain this combination than any change in the aorta.

12. While there is no unanimity of opinion as to the results of experimental work on animals, there are investigations, such as those of Sutton of Chicago, that seem to show that temporary occlusion of a coronary, a condition comparable to spasm, induces pain.

As I go back over this lecture to see what it is all about—is not that the way most papers are written?—I find that there is a thread of thought, rather slender at times I admit, that binds together the seemingly disconnected pieces out of which this paper has been constructed. The motif seems to be not so much to declare what we know concerning the coronary artery and its diseases as to point out certain gaps in our knowledge, certain problems that still await solution: the cause of arteriosclerosis and thrombosis; the pathology of chronic obstruction and its disease manifestations; the pitfalls of electrocardiography; the mystery of cardiac and especially anginal pain. At this point I might well, after the manner of the preacher or the commencement orator of other days, utter the perorational exhortation: "Let us then" realize that there is need for cooperation between the practitioner of medicine, the pathologist, the experimental physiologist and pharmacologist, the student of electrocardiography. Intensive, concerted investigation will surely bring forth rich results.

I am conscious also of harboring the thought and hinting at it in a tentative way that we should view the coronary lesions here described and the diseases caused thereby as one process rather than as several. Whether this process is acute or chronic, whether the lesions are slight or extreme, whether the results are mild or serious, there is a common unifying element—obstruction to the coronary flow. Klotz and Lloyd state the order of pathological events as endarteritis, atheroma, calcification, stenosis, thrombosis. We might add infarction and myofibrosis. If now we mix clinical and pathological features, we may slip into this list as we approach and leave thrombosis such terms as chronic or acute heart failure, ventricular fibrillation, sudden death.* And—I quote Le Count—"Somewhere between sudden occlusion and its results, and such slowly developing obstruction that few or no symptoms develop, lie the lesions responsible for angina pectoris."

In closing, much of our knowledge concerning the coronary artery and much of the present day interest can be traced to the impetus given

*Coronary obstruction and ventricular fibrillation seem to offer the most rational explanation of the sudden death in angina. There may be instances in which obstruction is complete without a thrombus. Usually, however, there is a thrombus. The clot, however, may easily be overlooked if death occurs before the more strikingly visible changes of infarction have taken place.

to the study of this subject by the observations of clinicians. Perhaps Scott is right when he says: "Medical history of the future doubtless will record as one of the important contributions to clinical medicine of the past twenty years the general recognition of coronary thrombosis." If this is so, it is one more argument to support the position so admirably outlined by Rufus Cole the other day before this body, that medicine—practical medicine—can now without apology hold up its head among the company of the physical and biological sciences that, while perhaps more exact, are not inspired by ideals more lofty, methods more honest or results more far reaching and beneficial. Without Dr. Cole's address, I should not have ventured to appear before you to present a paper so largely clinical. With his address I plucked up enough courage to accept the very kind invitation to deliver this Harvey Lecture, an invitation that I regard as a high honor and for which I thank you most sincerely.

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SERIAL ELECTROCARDIOGRAPHIC STUDIES IN CORONARY THROMBOSIS

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THE electrocardiographic changes produced by coronary occlusion have been a matter of keen interest during the past twelve years. In 1918 Smith[1] first made electrocardiographic studies in dogs in which he had experimentally occluded various branches of the coronary arteries. In 1920 Pardee[2] presented "an electrocardiographic sign of coronary artery obstruction" which he felt was diagnostic. In 1928 Parkinson and Bedford,[3] and in 1929 Levine and Brown[4] published their extensive studies in this disease. With the completion of this work, much data was available for an understanding of the electrocardiographic findings in coronary occlusion. It was at first believed that all cases would be associated with positive electrocardiographic changes, but instances have been disclosed of undoubted coronary occlusion in which no electrocardiographic evidence seemed present. To further complicate the picture, Scott, Feil and Katz[5] pointed out that positive ST changes in the electrocardiogram were sometimes present in pericardial effusion and in pericarditis. Kountz and Gruber[6] were able to produce experimental ST changes by the production of anoxemia. They did this by placing their animals in an atmosphere containing insufficient oxygen and also by powerful doses of a vaso-constrictor. More recently Shearer[7] has published a case of pneumonia in which positive ST changes were found in the electrocardiogram.

We believe that the above findings may all be explained on the basis of delayed coronary flow or the result of a general or local anoxemia; furthermore, it has been our impression that if more frequent electrocardiographic studies were made on undoubted cases of coronary thrombosis, it would be possible to demonstrate changes which might not be brought out by single or occasional tracings. With this object in mind, we have attempted to make serial studies on every case of undoubted coronary thrombosis coming to us in private practice during the last two and one-half years.

It has been our purpose to ascertain: (1) If any additional diagnostic criteria could be found by a more detailed study of such cases; (2) The degree of variability of the electrocardiographic waves found during the course of the disease; and (3) What if any prognostic significance could be attached to the various findings.

We have followed a total of twenty-four cases and in every instance, there has been electrocardiographic evidence of the disease. In the ac-

companying plates, thirteen of these cases are shown. Those not reported here, represent hearts in which only a single typical tracing was obtained before death, cases in which the study was incomplete, or tracings so characteristic as to be merely a repetition. We have not attempted to reproduce every tracing taken in a series, but have selected only those which were most significant. It will be noted that the tracings vary a great deal from time to time. If we rely only on the findings of a single electrocardiographic examination, such a tracing would be very misleading. This may be said to be particularly true if one is seeking only ST changes or the typical cove-shaped T-waves first described by Pardee. While both of these findings are of very frequent occurrence in coronary thrombosis, it is our feeling that they are by no means always present at the time a tracing is first made. It is only by serial study that evidence of the nature of the patient's complaint is obtained. The following is a summary of the electrocardiographic findings which we have found diagnostic of coronary thrombosis.

1. *Deflections from the Iso-electric Level of the ST or RT Interval.*—This finding when of real significance is usually quite marked and a deviation must always be present in at least two leads. It is sometimes found in three leads. In this series there is deviation upward in Leads II and III in five cases (1, 4, 5, 9, 13). There is deviation downward in Leads I and II in one case (2); upward in Lead I, downward in Leads II and III in two cases (3, 6); and in one case there is deviation downward in Lead I and upward in Leads II and III (10). The RT changes are of striking character in every instance with one exception, which is noted in Case 3. In this case there is very slight RT change upward in Lead I and downward in Lead II with some possible change downward in Lead III. It will be noted in this case that it was only after the end of forty-four hours that the slight ST change gave way to the cove-shaped T-wave in Lead I. In a few cases the RT deviation seems to reappear after the acute occlusion as in Cases 1, 4 and 5. As a rule however, the RT deviation usually disappears in a few hours or days and is replaced by the inverted cove-shaped T-wave or some other significant deviation.

2. *The Cove-Shaped Negative T-Wave,* sometimes called the "Pardee T-wave of cardiac infarction," appears frequently. However, in this series, there are two cases of proved coronary thrombosis in which a typical Pardee T-wave did not appear at any time even where tracings were taken a few hours after the onset (5, 8). In Case 8, an autopsy was available. An extensive infarction was present in the left ventricle, yet other changes than RT deviation or a Pardee wave were present in the electrocardiogram. In Case 3, the cove-shaped negative T-wave appeared in forty-four hours after the attack but in Case 6, the so-called typical T-wave did not appear for sixteen days. There are many variations between these two extremes. As has been pointed out by Parkin-

son and Bedford, the Pardee T-wave may entirely disappear after once being present. In this series it had entirely disappeared in four cases; in six months, ten months, twelve months and fourteen months respectively. In four cases the Pardee T-wave is still present at the end of eighteen months, twenty months, twenty-four months and thirty months, respectively.

3. *Changes in Amplitude.*—(a) The most frequent alteration occurs in the QRS complex, as has been noted by Wearn[8] and others. To be of diagnostic significance, this change must take place in a short period of time. It is frequently of marked degree and when the fall is extreme, may be interpreted as an indication of extensive myocardial damage. In cases in which the QRS fell to one or two millimeters, a grave prognosis has usually been substantiated. We have noted a marked fall in amplitude in seven cases (4, 6, 8, 13 and three cases not included in this paper).

(b) While a change in the T-wave is frequently demonstrated from hour to hour, or day to day in coronary occlusion, this fact has not been sufficiently emphasized. We believe that a marked flattening of the T-wave without other changes occurring in a brief period of time is also an indication of a sudden profound change in the integrity of the myocardium. We know of no process which can produce this sudden change except coronary occlusion. While the flattening out of the T-wave is usually associated with a lowering of amplitude of all portions of the curve, this is not necessarily true. In Cases 4 and 8, this marked flattening out of the T-waves is evident.

CASE HISTORIES

CASE 1.—A male physician, aged 65 years, had been in good health previously. His systolic blood pressure was usually 135-145 mm. On December 30, 1928, he had just awakened when he was seized with severe substernal and precordial pain. He became pulseless and cyanotic. A nearby physician who came found him in a state of collapse. After the administration of morphine, his pain was relieved and he complained only of weakness. He refused to stay in bed longer than two weeks and in three weeks he was walking outside. Since the attack he has remained quite well, but suffers stenocardia on walking fast or against a cold wind.

CASE 2.—A business man aged 69 years, who had suffered an attack of transient hemiplegia in 1918. His blood Wassermann was strongly positive at that time. He had received vigorous anti-luetic treatment when he would submit. On November 15, 1928, he was awakened at 5 A.M. by a severe precordial pain. When seen by us shortly afterward, he was pulseless, his extremities were cold and his blood pressure was below 100 mm. systolic. After the administration of morphine, and caffeine sodium benzoate, his condition improved. His convalescence was prolonged but uneventful. At times since then he has had attacks of severe weakness and a sensation as if he would faint. We considered these attacks due to his cerebral syphilitic endarteritis. More rigid specific treatment has stopped them. There has never been any evidence of aortitis or aneurysm in this case.

CASE 3.—A Jewish housewife aged 49 years. Her average systolic blood pressure was 210 mm. and she was markedly overweight. She also had a moderately large

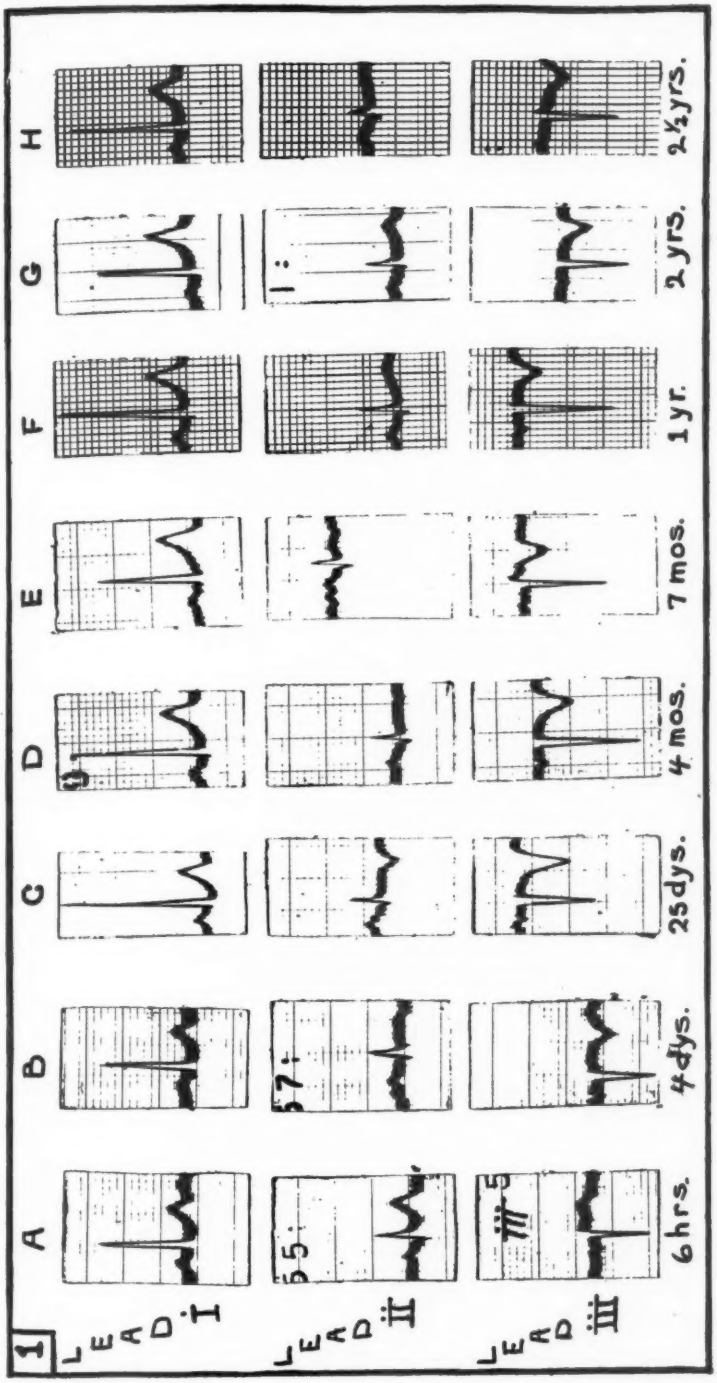

Fig. 1.—*A*, six hours after attack; *B*, four days after; *C*, twenty-five days after; *D*, four months after; *E*, seven months after; *F*, one year after; *G*, two years after; *H*, two and one-half years after. Note high take-off of RT in Leads II and III in *A*. The cove-shaped T-wave which develops in Lead II is gradually lost but T 3 remains deeply negative with a reciprocal high peaked and positive T 1. This is often a permanent residuum of coronary occlusion.

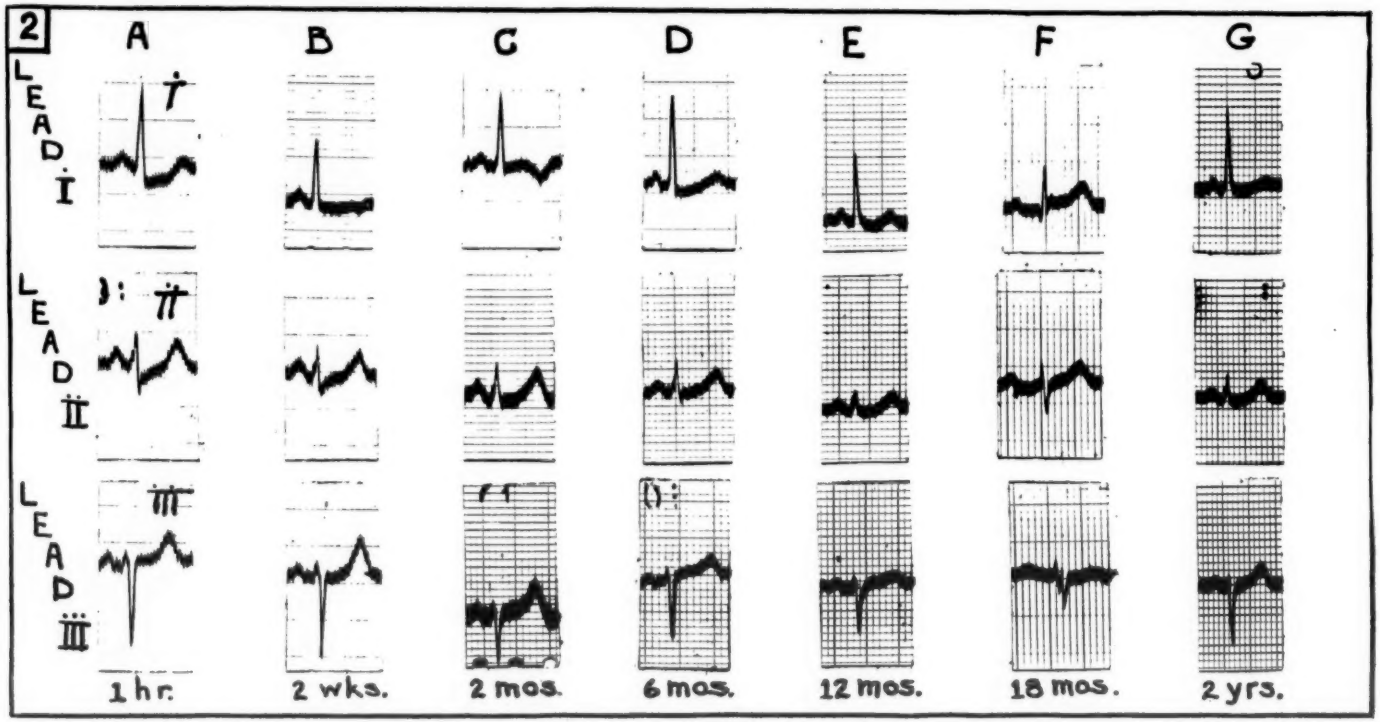

Fig. 2.—*A*, one hour after attack; *B*, two weeks after attack; *C*, two months after; *D*, six months after; *E*, twelve months after; *F*, eighteen months after; *G*, two years after. Note the positive RT changes in *A*. Here we find a cove-shaped negative T 1 appearing two months after the occlusion. The final tracing is normal in appearance.

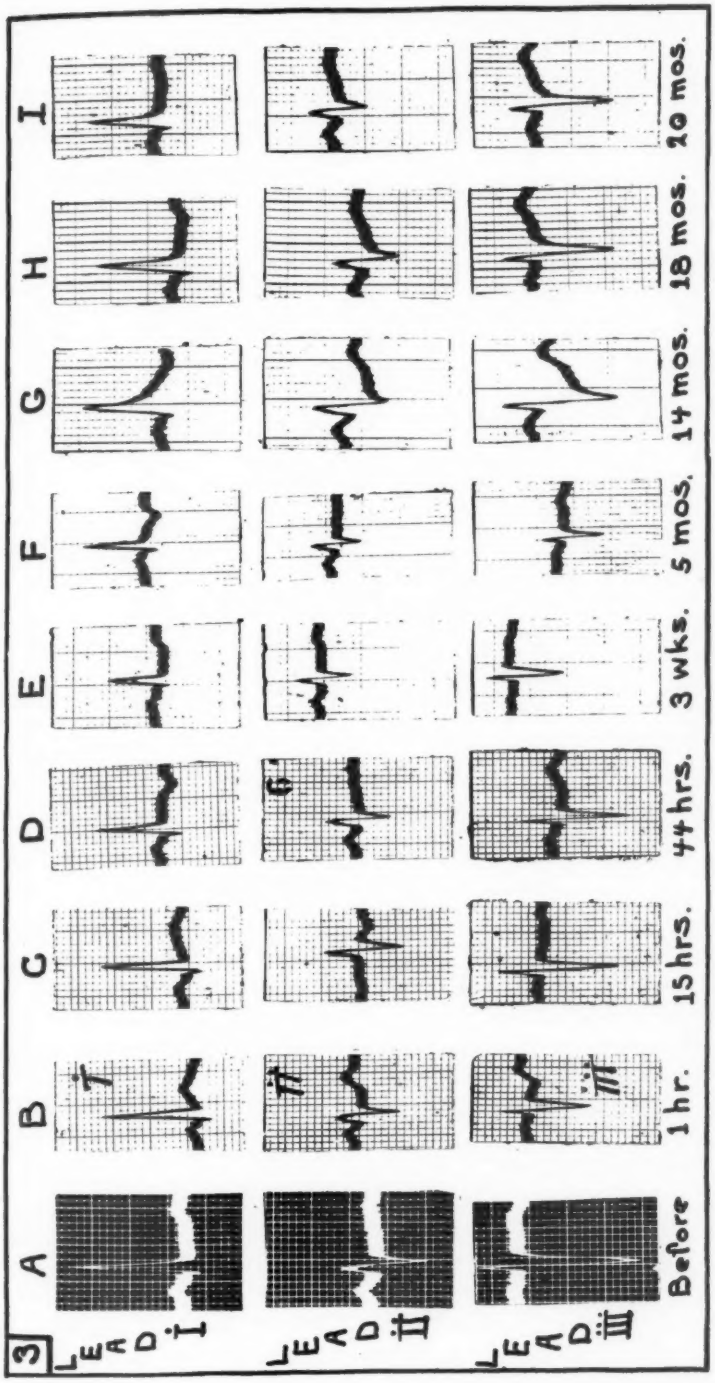

Fig. 3.—*A*, four months before attack; *B*, one hour after attack; *C*, fifteen hours after; *D*, forty-four hours after; *E*, three weeks after; *F*, five months after; *G*, fourteen months after; *H*, eighteen months after; *I*, twenty months after. Note the slight elevation of RT in Lead I and depression in Lead II in *B* and *C*. It is only at the end of forty-four hours that the cove-shaped T-wave appears. A flattening out of T 1 is noted, preceding the development of the cove-shaped negative T. *G* represents another small occlusion (see history).

thyroid adenoma and had taken thyroid extract at one time. At 4 A.M., March 28, 1929, she was awakened by substernal and precordial pain with radiation to the left arm. In a few minutes she vomited and insisted she was going to die. When seen in less than thirty minutes, she was pulseless, cyanotic and covered with beads of cold perspiration. Her blood pressure could not be obtained and there were numerous râles at both bases. After the administration of morphine (gr. ½) and caffeine sodium benzoate, her condition improved. For two days following, her temperature reached 100.5 in the afternoon. No friction sounds were heard. Fourteen months later she had another mild attack for the relief of which a total of one grain of pantopon was required. On exertion she still complains of stenocardia and her systolic blood pressure is above 200.

CASE 4.—A general insurance agent aged 53 years. Fourteen months before he had suffered an attack of chest pain and subsequent fever. Coronary thrombosis was not diagnosed at that time. He was seen four weeks later by another physician who took an electrocardiogram and insisted that the patient give up his work for one year. Three days before he was first seen by us, he avoided an automobile accident only by strenuous effort on his part. Following this near accident, he felt some chest discomfort and decided to have a physicial examination. He was ordered to bed but two days later we were called in emergency to his home where we found him suffering intense substernal pain. He was cold and already marked cardiac decompensation was present. His condition was grave for two days following this, but improvement occurred and he seemed to be progressing very satisfactorily. Signs of cardiac failure reappeared and five days following the onset of severe pain he died. Autopsy revealed an old and partically canalized thrombosis of the right descending coronary, a large infarction of the anterior wall of the left ventricle and a fresh thrombosis of the descending left coronary artery about 2 cm. from its union with the left circumflex artery. The coronary vessels were not markedly sclerosed as a whole but at the site of the fresh thrombus, marked calicification was present for a distance of 1.5 cm.

CASE 5.—Automobile executive aged 39 years. He had rheumatic fever for three months at the age of 14 years, but considered himself unusually well. Two years previously, a general physical examination failed to reveal any abnormality of heart or blood pressure. On the morning of August 16, 1929, he was awakened by severe precordial pain of great intensity which radiated to both shoulders and down both arms to his finger tips. He said he felt as if he were going to die. After two hours, however, he had only dull pain and was finally driven to the factory where he was again seized with severe pain and collapsed. He was given morphine and when his condition permitted, he was taken to the hospital. At entry six hours after the onset of pain, his temperature was 100 and his pulse 100. The total white blood count was 19,200. Physical examination revealed very faint heart sounds and a blood pressure of 110 systolic and 80 diastolic. The following day a friction sound was audible over a limited area at the fourth interspace to the left of the sternum. In 48 hours his temperature was normal and he felt very little discomfort. Five weeks after the onset he insisted on going to the bathroom after which precordial pain recurred. For the first time râles were audible in both bases. A more prolonged convalescence was uneventful. He now is moderately active and free from pain.

CASE 6.—Real estate man aged 53 years. He had been a very heavy smoker all his life and at times a heavy drinker. Following a drinking bout in 1929, his blood pressure was found to be 170 systolic and 100 diastolic, but subsequently never exceeded 150 systolic. His apartment was on the fourth floor but in spite of the fact that there was no elevator, he did not complain of cardiac symptoms. On the evening of October 12, 1930, he was lifting a heavy trunk when he felt

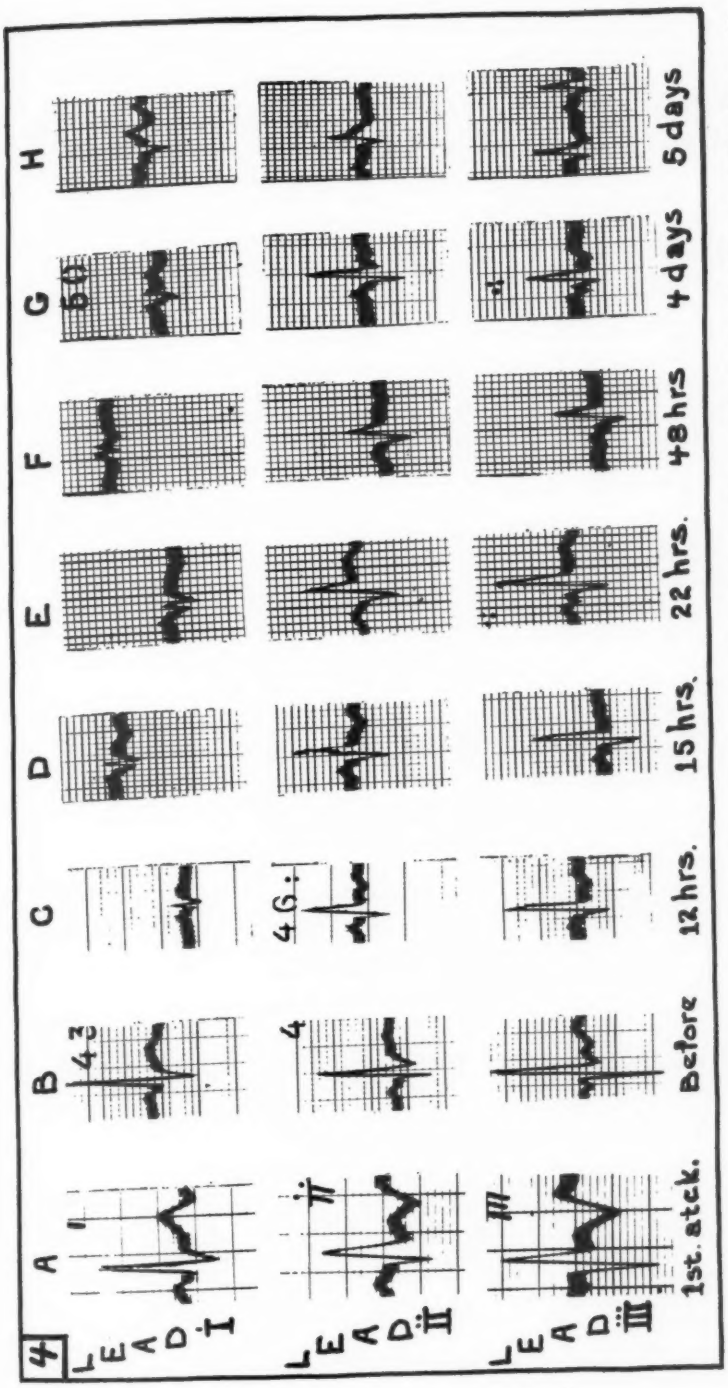

Fig. 4.—*A*, three weeks after first attack; fourteen months before fatal attack; *B*, two days before collapse; *C*, twelve hours after collapse; *D*, fifteen hours after collapse; *E*, twenty-two hours after collapse; *F*, forty-eight hours after collapse; *G*, four days after collapse; *H*, five days after collapse, and three minutes before death. Note recovery following the first occlusion. The marked fall in amplitude of QRS in Lead I after the fatal complete occlusion is striking. The variability from day to day is of interest in this case in which we find RT changes, flattening of T-waves, fall in amplitude of QRS and cove-shaped negative T-wave, all represented at one time or another.

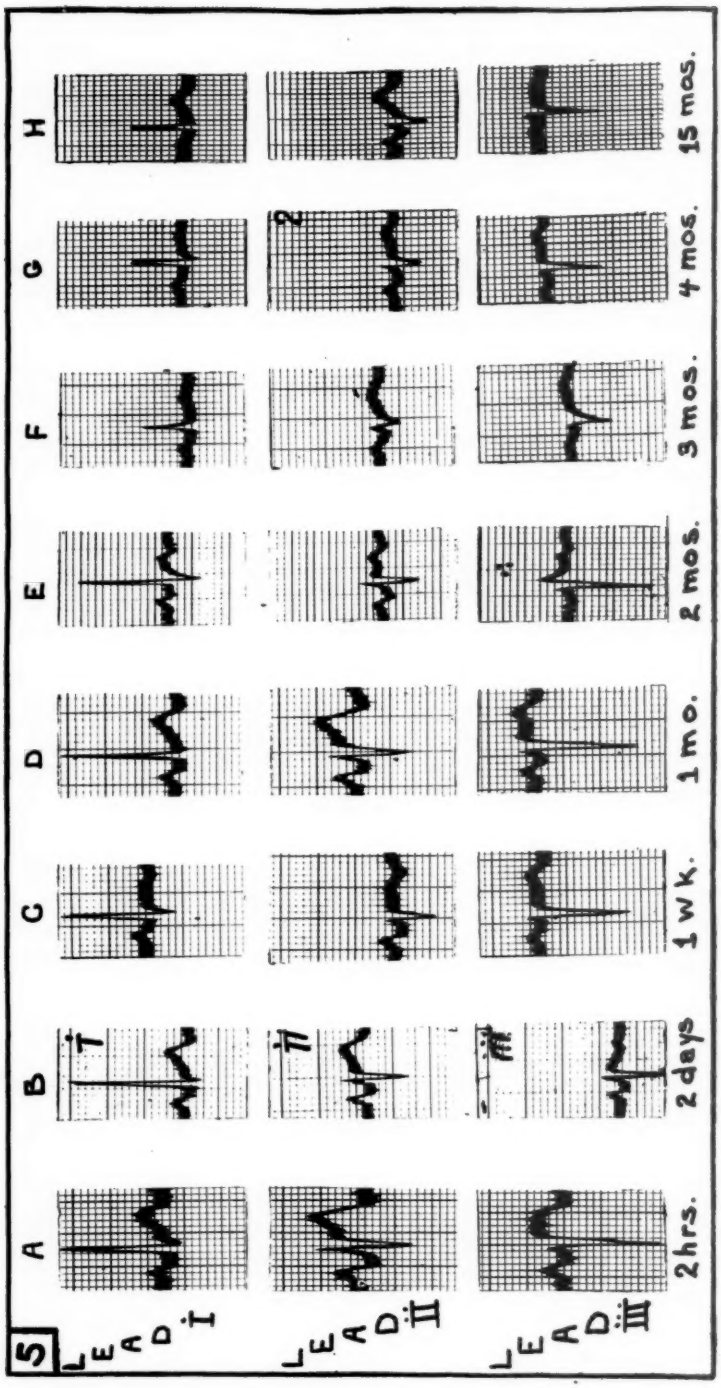

Fig. 5.-*A*, two hours after complete collapse; *B*, two days after; *C*, one week after; *D*, one month after; *E*, two months after; *F*, three months after; *G*, four months after; *H*, fifteen months after. Note in *A* the high take-off of ST. This is lost but reappears one and two months after the occlusion. A diphasic slightly cove-shaped T 1 and T 2 is present one week after the attack but does not appear thereafter. The great variability of findings are well shown.

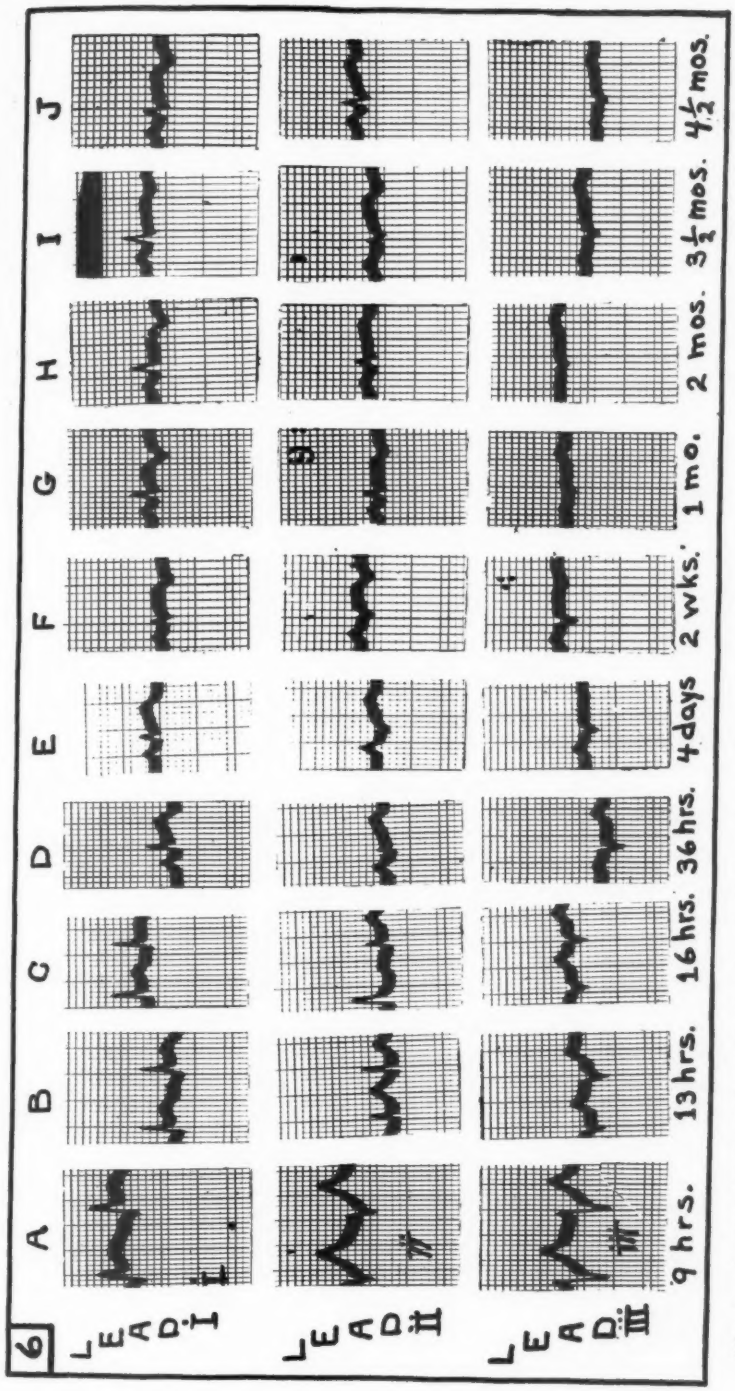

Fig. 6.—*A*, nine hours after onset of pain; *B*, thirteen hours after; *C*, sixteen hours after; *D*, thirty-six hours after; *E*, four days after; *F*, two weeks after; *G*, one month after; *H*, two months after; *I*, three and one-half months after; *J*, four and one-half months after. Note the typical RT elevation in the early curves and the rapid fall in amplitude of the QRS. The cove-shaped T-wave in Leads I and II does not appear for sixteen days after the occlusion and has not disappeared in Lead I at the end of four and one-half months. This is the only case in which the voltage has fallen as low as is found in *F*, that has survived the attack.

some chest discomfort. This slowly increased and at 1:00 A.M., October 13, he walked downstairs and to a near-by hospital where the night doctor examined him but found nothing of significance. One grain of codein was given but without the slightest benefit. At 6:00 A.M. after five hours of agony, one of us was called to see him. He did not in any respect seem acutely ill. His color was good, the pulse 100, blood pressure 140 systolic and 90 diastolic. The heart sounds seemed as usual and there was no pulmonary congestion. He had no rise of temperature. One-fourth grain of morphine was given but in thirty minutes he was no better so that the dose was repeated with gradual relief. He localized the pain in the region of his sternum at about the level of the fourth interspace; there was no radiation. Entirely on the basis of the intensity of his pain, coronary thrombosis was diagnosed. During the first forty-eight hours his condition became critical. His temperature averaged 100.5 for four days. After this he felt very well. He was not allowed out of bed for ten weeks. His condition is very satisfactory at the present time, although he has not been allowed to leave his rooms.

CASE 7.—A housewife aged 59 years. She had had epileptic seizures for many years but of very infrequent occurrence. At times she complained of some dyspnea on climbing stairs but physical and electrocardiographic examination was normal. On the evening of April 2, 1928, she was alone in her home when burglars entered and at the point of a gun tied her to the bedpost. After they had looted the house, she released herself and ran screaming to her neighbors. After much excitement, she retired at 1 A.M. but one hour later had an epileptic seizure. She appeared very weak so a physician was called who found her almost pulseless. On the following day she had a very irregular pulse, a temperature of 101 F., and profuse râles were found in both bases. For three days she complained of slight pain just beneath her clavicle on the left. Four days elapsed before coronary occlusion was diagnosed and then only after the electrocardiogram was seen. At the present time she has some palpitation and dyspnea on climbing stairs, but no precordial pain.

CASE 8.—A business man aged 70 years had complained of bronchitis for many years but had been unusually active and well. Following coitus on June 22, 1930, he felt some chest discomfort and by the next morning, this had increased. Morphine was finally required for relief, although his distress was not well defined. His blood pressure gradually fell to 100/60, the heart sounds were very faint and râles appeared in both bases. His condition grew gradually worse, but after three days was much improved and he felt well. His blood pressure remained between 90 and 100 systolic. The heart sounds improved and the râles disappeared from the chest. His temperature reached 101° F. during the first three days. On the second day after the onset, his white blood count was 18,000. On the morning of the seventh day as he was about to eat his breakfast, he suddenly clutched his throat and was dead in a very few seconds. At autopsy the coronary vessels were found to be markedly sclerosed throughout and there was a softening thrombus completely occluding the left descending branch. There was an extensive infarction of the left ventricle.

CASE 9.—Female, aged 70 years. She had complained of precordial and chest pain after excitement or exertion since November, 1928. Physical examination and electrocardiogram revealed no abnormalities but the blood pressure was 170 systolic and 90 diastolic. April 3, 1930, she complained of vise-like pain which came on after attending a moving picture. Again examination revealed nothing. May 1, 1930, while visiting in Pittsburgh, she was seized with precordial pain which required morphine every three hours to control. On May 23, she returned to Detroit where we noted an alteration in the electrocardiogram (Fig. 9-*B*). She remained quite well although she often complained of heaviness across her chest. On Novem-

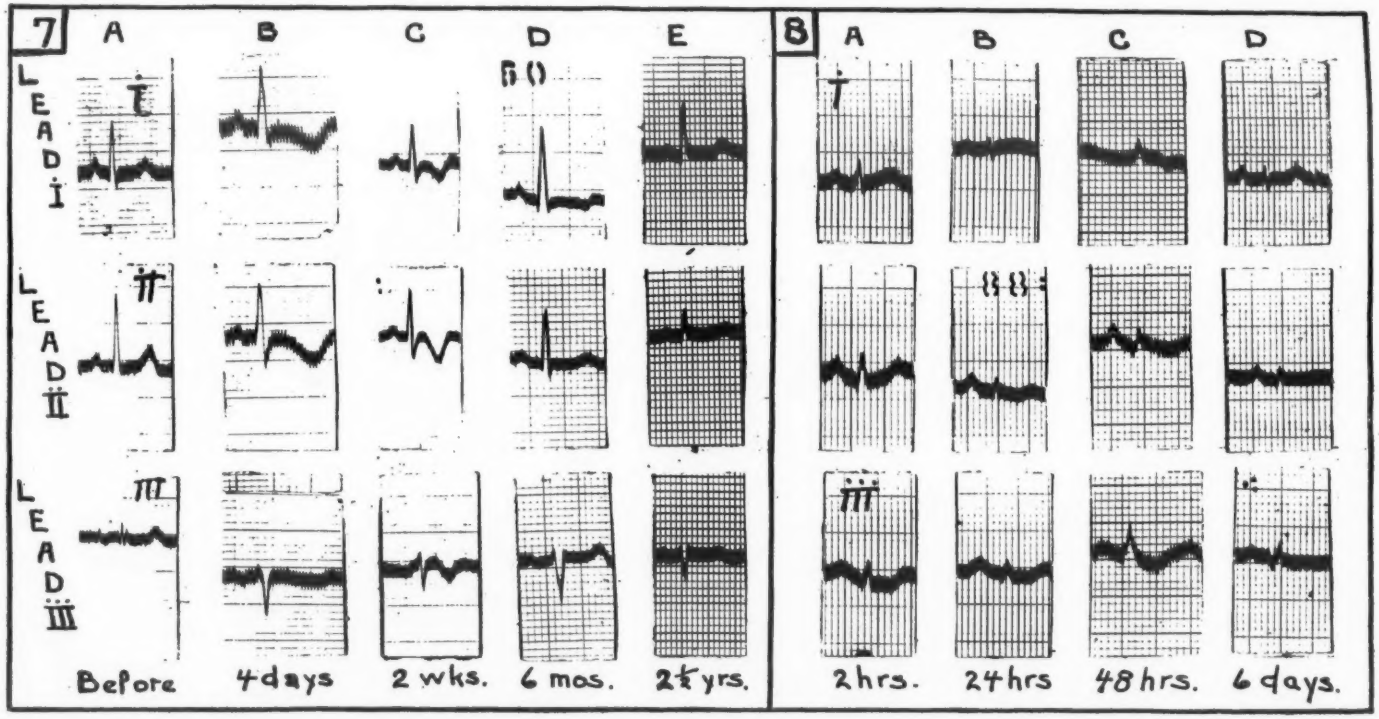

Fig. 7.—*A*, six months before attack; *B*, four days after attack; *C*, two weeks after attack; *D*, six months after attack; *E*, two and one-half years after attack. Note the deeply negative cove-shaped T-waves in *B* and *C*. This is a typical cove-shaped T-wave type of curve.

Fig. 8.—*A*, two hours after attack; *B*, twenty-four hours after attack; *C*, forty-eight hours after attack; *D*, six days after attack; twelve hours before death. Note presence of T-waves of nearly normal amplitude in *A*. In this case the T-waves flatten out in a very short time as the case progresses. The amplitude of the QRS also diminishes rapidly and reaches a low level. The patient's attack was not typical and entirely on the basis of the rapid changes in the T-waves and the rapid fall of QRS amplitude, a presumptive diagnosis of coronary thrombosis was substantiated.

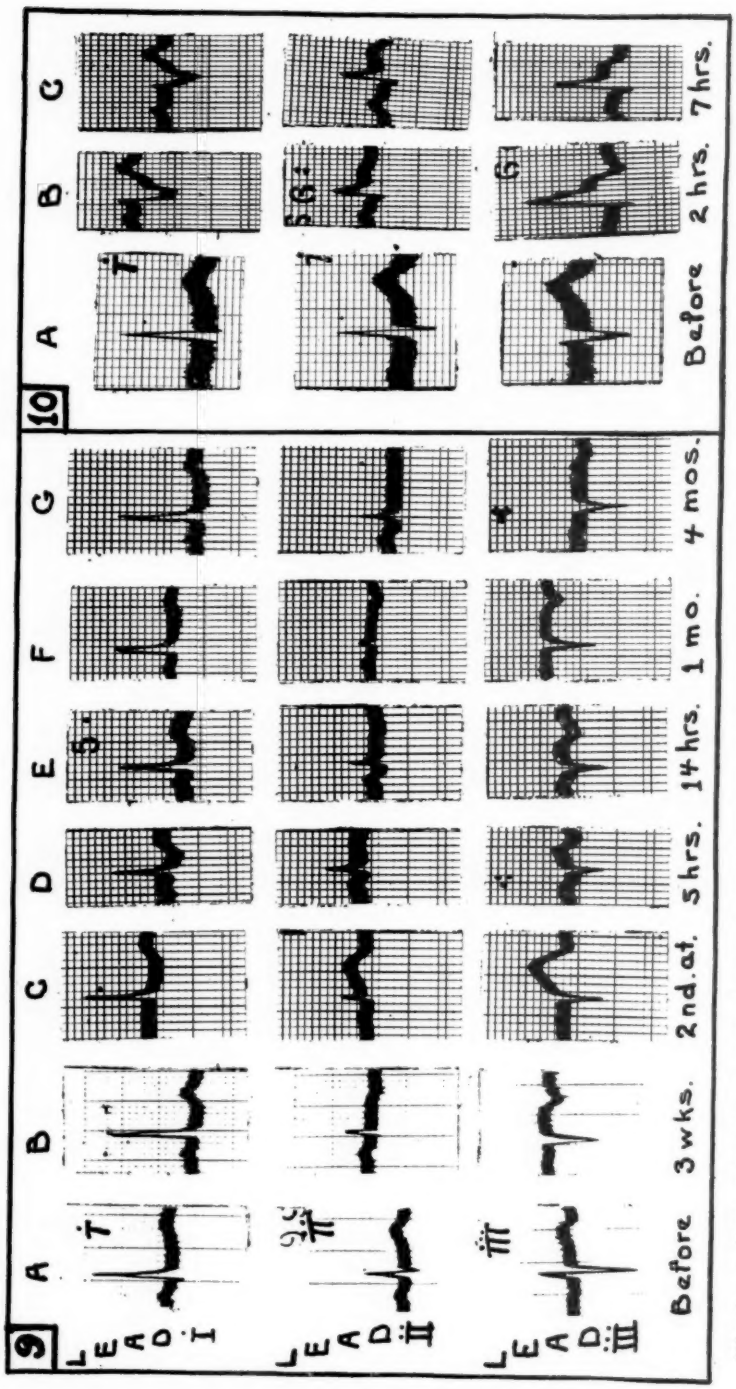

Fig. 9.—*A*, three weeks before first attack; *B*, three weeks after; *C*, during second attack; *D*, five hours later; *E*, fourteen hours later; *F*, one month later; *G*, four months later. The change in T 3 with a slightly higher and sharp T 1 is the only residuum of the first attack. In this series the RT changes are unmistakable and characteristic. Only at the end of thirty days does a cove-shaped T 2 appear following the second infarction.

Fig. 10.—*A*, one year before attack; *B*, two hours after attack; *C*, seven hours after attack, four hours before death. Following the occlusion the typical RT changes are produced. The PR and QS intervals also are prolonged. In this series note RT and ST changes of striking degree in every lead.

ber 1, she began to have precordial pain with radiation to the left arm especially involving the left thumb. The pain was so intense that she insisted she was dying. When first seen in this attack, she was slightly cyanotic, her pulse was 100 but perfectly regular. The blood pressure was 90 systolic and the lungs clear. Her condition rapidly grew worse and in twenty-four hours her temperature had risen to 100.8 degrees F. and her total white blood count was 12,000. Râles were never detected in the lungs and a friction sound was never audible. In four days she was comfortable although she complained of great weakness. She is still convalescing.

CASE 10.—A business man, aged 70 years. He had complained of precordial pain for two years and his blood pressure was usually 180 systolic and 100 diastolic. He frequently used nitroglycerine for the relief of the stenocardia. On the morning of October 11, 1930, he was awakened at 5:00 A.M. with severe pain in his chest. When seen he was sitting up in bed presenting the appearance of extreme anguish. His color was ashen, the blood pressure below 100 systolic, there were profuse râles in both bases and the pulse was rapid and weak. His condition slowly grew worse and fourteen hours after the onset of pain, he died. An autopsy was not obtained.

CASE 11.—A drug salesman, aged 50 years. In 1924 he was seen complaining of joint pains. At that time a systolic murmur was heard at the apex and aortic area. The blood pressure was 155 systolic and 90 diastolic. The blood Wassermann was negative. In February, 1928, he consulted us because of a dull discomfort across the upper chest which he thought was related to exertion. There was some radiation of the distress to both shoulders and arms. At this time a definite to-and-fro murmur was heard over the aortic area and the supracardiac dullness was increased. The Kolmer Wassermann was 1-3-3-0-0. He was given anti-luetic treatment for a time and was definitely improved. In September, 1928, he began to complain of precordial pain on exertion. On September 25, 1928, he was seized by excruciating and vise-like pain in the arterior chest, and was unable to get out of bed. Morphine was required for twelve hours and the following day the temperature was slightly elevated. At the present time he has stenocardia on strenuous exertion but the aortic widening and the to-and-fro murmur are unchanged. His blood pressure in December, 1930, was 120 systolic and 80 diastolic.

CASE 12.—Merchant, aged 62 years. For three years he had complained of stenocardia on exertion and had been told that he had high blood pressure and nephritis. September 24, 1930, he began to have precordial pain which was more persistent and more severe than ever before and which was not entirely relieved by nitroglycerine. His blood pressure on October 7, 1930, was 170 systolic and 100 diastolic, the heart sounds were very weak and there were râles at both bases. From then on his pressure began to fall and in two weeks had fallen to 100 systolic. There were more râles at the bases. Though he often would go several days without any precordial pain, he had three attacks of great severity. On November 10, 1930, he was awakened at 5:00 A.M. by an intense difficulty in breathing which his relatives described as of a "rattling" character. He could hardly speak and was in great anguish. In less than ten minutes he was dead. Autopsy was refused.

CASE 13.—Retired realtor, aged 75 years. For eight years he had complained of attacks of chest pain following exertion and had used nitroglycerine with some relief. On October 23, 1930, he complained of a steady and intense precordial pain which nitroglycerine did not relieve. When examined a few hours after morphine had been given, he was very comfortable, the pulse was 110, the blood pressure 100 systolic and 60 diastolic and the heart sounds of fair quality. The lungs were clear. On the following day râles were heard at the base of the lungs. He often

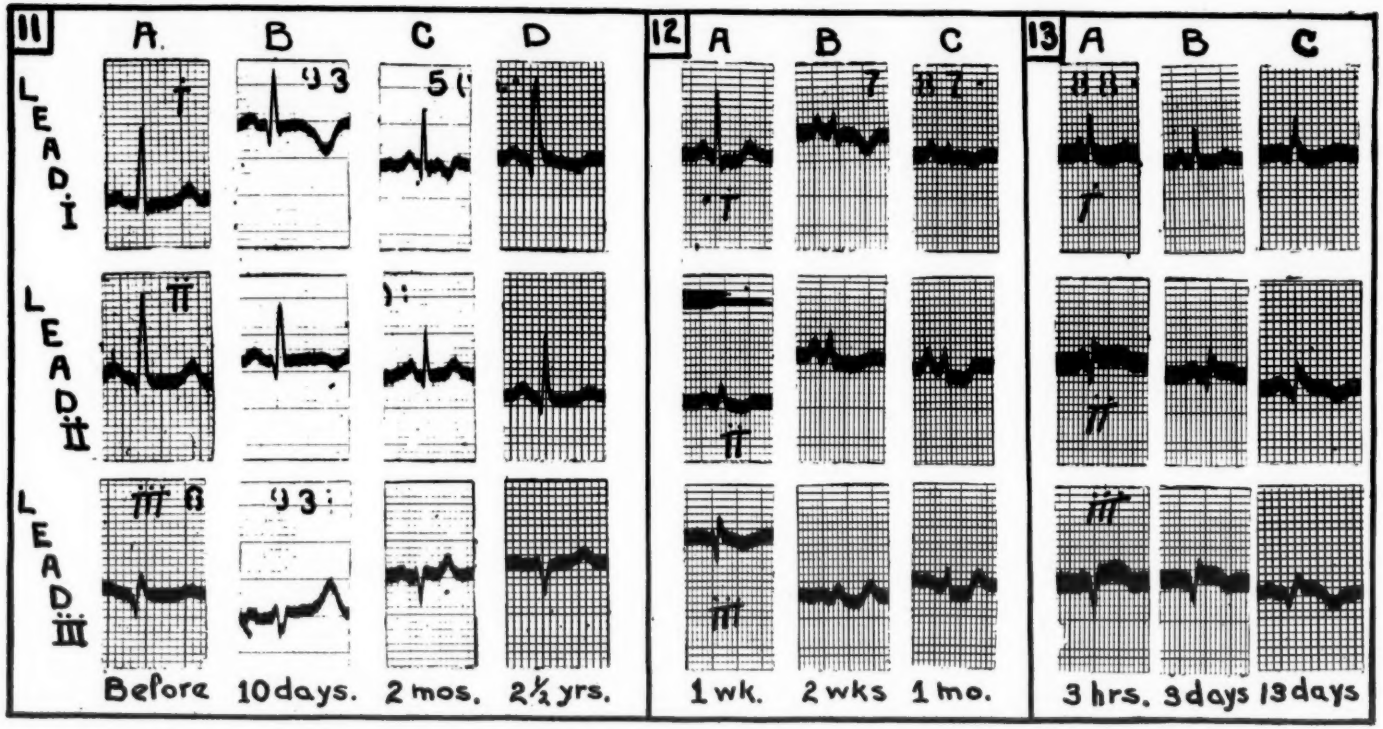

Fig. 11.—*A*, three and one-half months before attack; *B*, ten days after attack; *C*, two months after attack; *D*, two and one-half years after attack. The reciprocal T 1 and T 3 of magnified amplitude, as compared with the previous curve, is apparent in *B*. At the end of two and one-half years the T 1 change is the only residuum.

Fig. 12.—*A*, one week following first persistent pain; *B*, two weeks after; *C*, one month after and five days before sudden death. The progressive changes are evident in this case; the occlusion was either a slowly increasing one, or multiple occlusions. The falling amplitude indicated a poor prognosis.

Fig. 13.—*A*, three hours after attack; *B*, three days after; *C*, thirteen days after and one week before sudden death.

required morphine for relief of pain during the first week of this illness and afterward for restlessness. His condition steadily failed and he died three weeks after the onset of his severe pain.

COMMENT

While we are not prepared to say that characteristic electrocardiographic changes always occur following acute coronary occlusion, nevertheless it would seem that when serial studies are made, the proportion of positive findings is extremely high. In twenty-four consecutive cases studied serially, thirteen of which are shown herein, there have been positive electrocardiographic changes present in every case. As has been frequently shown in the past, the most common changes are RT deviation and the cove-shaped negative T-wave. The RT deviation has occurred in eleven out of sixteen cases and the cove-shaped negative T-wave has occurred in twelve out of sixteen cases.

Aside from the two more frequent findings just mentioned, we should like also to emphasize the importance of a marked fall in amplitude of the QRS complex. When there is available a previous curve for comparison, or when a marked fall occurs in a few hours' time, then coronary occlusion with subsequent myocardial softening may well be suspected. In this series a marked fall in amplitude is noted in seven out of sixteen cases. In one case it was of very real diagnostic benefit (8), for the onset of the patient's illness was not typical and when first seen he did not seem gravely ill. The first electrocardiogram, however, revealed an irregular rhythm and very low QRS voltage. In less than twenty-four hours this low amplitude dropped to a lower level. After remaining low for six days the patient seemed clinically well but died suddenly on the seventh day of his illness.

Changes in the T-wave were very frequent in the course of this serial study. Before a typical cove-shaped negative T-wave appears, there often occurs a flattening out of the T-wave. When there is a marked fall in amplitude of the QRS as in Cases 4 and 8, the T-wave suffers similarly by its flattening out. We feel that such a change occurring in the course of a few hours can only mean sudden profound damage to the myocardium. Acute coronary occlusion with infarction is without question the most common cause of such an event. Usually a poor prognosis is indicated where a marked fall of amplitude of the QRS either persists at a very low level or is constantly progressive beyond the first week or ten days. Four such cases were observed and only one of them (6) has survived.

SUMMARY

Serial studies were made on twenty-four cases of acute coronary occlusion. Positive electrocardiographic evidence is present in every case. The importance of taking consecutive electrocardiograms in suspected cases is emphasized. The changes of diagnostic significance are:

1. Deviation of the RT or ST interval. This change occurred in 11 of sixteen cases.

2. Development of the cove-shaped negative T-wave, first described by Pardee. This change occurred in twelve of sixteen cases.

3. Marked fall in amplitude of the QRS complex in a short space of time. This occurred in seven of sixteen cases.

4. Flattening out of the T-wave in a brief period of time. This change occurred occasionally preceding the development of the cove-shaped negative T-wave. It was marked in two cases which did not develop the typical cove-shaped T.

When a marked or progressive fall in amplitude of the QRS complex is seen, a poor prognosis is strongly suggested. Four cases revealed such a change and only one has survived the attack.

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FACTORS FAVORING THE ONSET AND CONTINUATION OF RHEUMATIC FEVER*†

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DURING the past three decades our ideas concerning rheumatic fever have undergone striking evolution, as evidenced by the change in nomenclature from acute articular rheumatism to acute rheumatic fever, and finally to rheumatic fever. True it is that the older terms still hold, and rightly so when used to describe particular forms of the infection; but too often one is employed synonymously with another. It is unfortunate that with increasing knowledge of the condition there cannot be devised a new term sufficiently extensive to embrace all of its manifestations, yet distinctive enough to separate it as a nosological entity. The introduction of the terms "infectious rheumatism"[1] and "rheumatic granulomatosis"[2] are attempts in this direction; but having only pathological or bacteriological significance they offer little if any advantage over the term rheumatic fever, which at least has background in clinical experience.

Objections to the use of this term are twofold: (1) The adjective "rheumatic" to most persons signifies arthritis or muscular pain, and (2) some of the manifestations of activity—notably chorea—are frequently not accompanied by fever. To this one may reply, first, that the original meaning of the term "rheuma" was a morbid process flowing from one organ or tissue to another; hence it still retains its descriptive value; and, second, that regular consistent use of the thermometer would reveal some degree of pyrexia during certain periods of most attacks; therefore, fever still remains one of our most valuable guides of persisting infection.

Another point deserves attention; if the term rheumatic fever is substituted merely for the expression, acute articular rheumatism, our nomenclature has suffered a loss, because the second signifies acutely swollen joints. When, on the other hand, it is used to include all of the manifestations of the infection in the same manner as tuberculosis includes all types of the disease induced by the tubercle bacillus, then does it have distinct descriptive value.

To many it seems well to delete the word acute because in the majority of cases the infection is long-standing. Only when rapidly fatal, or in those cases with a monocyclic course may the adjective

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"acute" be properly applied, but even then we must be certain that the infection has become permanently inactive. For example, we do not picture syphilis as acute even though the roseola disappears within two weeks; likewise it may be better not to use any single manifestation of rheumatic fever as an index of chronicity.

Historically the conception of rheumatic fever began with rheumatic polyarthritis; a century has elapsed since the recognition of the importance of involvement of the valvular endocardium; fifty years ago the nature of the subcutaneous nodule was noted; twenty-five years later its analogue in the submiliary myocardial nodule—the Aschoff body—was described; and within the past decade the extent of the vascular lesions has been appreciated. In the meantime with an improvement in the general economic state of society, together with extensive use of salicylates, the clinical picture has apparently changed. Hyperpyrexia rheumatica has become a medical curiosity, and according to old clinicians rheumatic polyarthritis is less severe. But whether there has been a corresponding amelioration in carditis and chorea one may well doubt. Knowledge gained from contemporary graphic methods of recording cardiac abnormalities renders difficult comparison with statistics obtained in other ways; but figures such as presented by Ehrström and Wahlberg[3] in Helsingfors indicate that there has been no diminution in the incidence of chronic rheumatic heart disease from the administration of salicylates; and according to recent statistics it still seems that rheumatic fever is the largest single factor in the causation of heart disease.[4]

May it not then be of greater value to apply another method of historical approach, beginning in childhood and following the various manners of the unfolding of the infection, rather than to orient ourselves from the disease in adults where it is less frequent even though more acute, and where severe cardiac damage is relatively less common.

But before tracing the clinical course it may be well to reconstruct a background of histopathological tissue changes. What does the microscope show us concerning the nature of the infection? Aschoff's description of the submiliary nodules arising in the loose connective tissue septa in the myocardium furnished a structural archetype to which alterations in other tissues might be compared. The discussion which has centered about this nodule has at times diverted attention away from the fact that other lesions, possibly not quite so regular in their cellular structure, might be just as characteristic. One need only mention the subcutaneous nodule. The important factors to recall are the type of tissues and organs involved, and the manner of evolution of the lesions; one may then attempt to construct from these factors or elements a hypothesis of the nature of the infection.

In the Aschoff body there is a minute central area of broken collagen fibers, surrounded by large cells probably derived from locally stim-

ulated connective tissue. At times there are seen polymorphonuclear cells, lymphocytes and plasma cells; and finally fibroblasts leading eventually to a scar. The subcutaneous nodule shows qualitatively similar tissue injury and cellular response, but with different quantitative distribution of the component parts; the connective tissue degeneration is often more massive, the groups of large mononuclear cells are more numerous. Frequently a large nodule is apparently formed as a conglomeration of smaller nodules. In places large basophilic mononuclear cells seem to arise from vessel walls. Relatively few polymorphonuclears are present. If now we examine the joints another but related picture appears. The peri-articular tendons and ligaments show numerous microscopic areas in form of nodules or tongues, most having necrotic centers and surrounding proliferated cells. The synovia shows palisading of its lining layer, and minute foci with central necrosis with surrounding collars of cells. Diffuse infiltrations of polymorphonuclears are common. The peri-articular tissues are infiltrated with serum which in part contributes to the familiar swollen joint; and there is destruction of muscle fibers at the musculo-tendinous junctions.[2, 5, 6] In other words, the minute focal and vascular lesions about the joints are numerous, and exudation is widespread. Involvement of the pleura and pericardium shows similar exudative tendency, but in the substance of these membranes are often foci comparable with the Aschoff bodies. In the auricular endocardium there are similar tissue and cellular changes, but these are arranged in streaks and plaques without interruption in the continuity of the lining endothelium.[7, 8] In the valves on first sight appears another picture, for the endocardium is broken and thrombotic verrucae are often, though not always, laid down at the site of impact of the leaflets. But throughout the substance of the valve and in the chordae may often be seen broken collagen material, proliferative cells and infiltrations like that of the auricular endocardium; at times they are arranged in typical Aschoff bodies. As so beautifully shown by von Glahn and Pappenheimer[9] and others, many portions of the vascular system are similarly involved. In the aorta focal lesions follow branches of the vasa vasorum; but smaller arteries have areas of end- and mesarteritis, always accompanied by focal destruction of connective or elastic tissue. In the peritonsillar, nasopharyngeal and intestinal blood vessels Holsti[10] has demonstrated extensive endarteritis verrucosa. In the peritonsillar capsule near the points of attachment of the pharyngeal muscles MacLachlan and Richey,[11] Gräff[12] and others have described areas very similar to Aschoff bodies, and also in the tongue about the lingual tonsils. Gräff applies the term "primary complex" to these peritonsillar lesions because of their hypothetical rôle as sites whence the infectious agent is distributed to other parts of the body. He thinks that the pathological condition of the blood vessels supplying these lesions favors such a distribution.

The striking picture of the Aschoff body cells has, moreover, attracted attention away from what appears to be the initial injury to the connective tissue fibers. Von Glahn and Pappenheimer have frequently described the granular broken appearance of these fibers, and many have seen the fibrin-like staining infiltration in the foci; but recently Klinge[13] claims that the primary change is a minute focal "fibrinoid swelling" of the intercellular mesenchymal ground substance; which swelling leads secondarily to a fraying out and altered staining reaction of the collagen fibers and fragmentation of the elastica. He also describes waxy degenerations of individual muscle fibers with secondary proliferation of the perimysium.

It thus appears that rheumatic fever instead of affecting any one set of organs is a disease primarily of the connective tissue, or, in Hueck's[14] words, of the mesenchymal system. Those structures composed chiefly of connective tissue, and specially subject to functional stress and strain and undergoing active motion appear to be the most vulnerable. Interference with the function of these moving structures may, however, detract attention from unobtrusive lesions in other organs, such as recently described by Paul[15] in a rheumatic perihepatitis with characteristic lesions in the underlying blood vessels. Rheumatic vasculitis in the kidneys has been described by Fahr,[16] Evans[17] and others; and symptoms of appendicitis, intimately associated with generalized rheumatic fever, point to a similar involvement of at least one portion of the intestinal tract. A constantly growing literature on pulmonary lesions in this disease indicates also how the lower as well as the upper portion of the respiratory tract may be involved.

A knowledge of the numerous points and tissues where the infectious agent attacks the body gives us another standard with which to judge rheumatic fever. If so many organs or tissues are simultaneously involved, there is every reason to suppose that they may also be individually and successively implicated. In fact, pediatricians have long appreciated the tendency of children to show first one and then another of the so-called rheumatic series;[18] and that not until after the lapse of years might enough members of this series have appeared to render certain a diagnosis. Monosymptomatic signs of disease are difficult of interpretation unless sufficiently characteristic to have diagnostic specificity; for example, the various cutaneous syphilides. But in order to form correct judgment concerning visceral lesions it is often necessary to have concomitant clinical signs or specific laboratory aids.

Unfortunately in the case of rheumatic fever no specific laboratory test is at hand; some of the concomitant, easily visible manifestations, such as tonsillitis, are too nonspecific to furnish much needed assistance. But in these very nonspecific signs we may possess most important aids to understanding the nature of the infection; and in tracing the life

history of rheumatic fever it is essential to note their occurrence and then try to interpret their influence upon the course of the malady.

The causation of many chronic diseases is usually the algebraic sum of a number of factors rather than the exclusive action of any one. Infection is the result of interaction between an animal host and an infecting parasite in which many variables are too subtle for laboratory measurement. Moreover, the study of the life history of chronic disease in the patient gives us many useful hints as to the nature of the illness, and often furnishes therapeutic indications. For example, we now know that the presence of tubercle bacilli in a body does not necessarily indicate active tuberculosis. Certain environmental conditions favor the spread of the lesions; others favor their regression. Indeed, a study of these latter conditions has furnished us with some of our most important weapons against this disease; and comparable knowledge may conceivably have a similar effect in rheumatic fever.

Geographically the disease seems to be essentially one of the temperate zone. Clarke[19] has recently marshalled most convincing evidence indicating that in the true tropics it is fifteen to twenty times less frequent than in Europe. Studies by the Seegals[20] indicate, moreover, that the infection is less common in the southern part of this country; and observations[21] from New Orleans show that when present in the South it runs a milder course than in the North. The ultimate effect of removing rheumatic subjects to hot or dry climates is, however, still a matter for investigation.

Statistics also show that obvious rheumatic fever is from fifteen to twenty times more frequent among the laboring classes than in those forming the bulk of private practice. But many physicians can testify concerning its existence and tendency to progress in patients living under apparently ideal home surroundings. Another viewpoint has been advanced to the effect that among persons in better economic conditions the infection may have relatively more monosymptomatic forms and hence lead more frequently to cardiac damage without obvious general symptoms.

Infants and very young children are relatively free from the disease, and, even though cases appear in children of from two to four years, the curve of frequency of first attacks does not begin its steep ascent until about the age of five or six years. It then rises steadily until the period from nine to eleven years when it begins to fall. First attacks are relatively much more rare in adults than in children. The studies of Wilson, Lingg, and Croxford[22] indicate, moreover, that children suffering from the infection tend to have fewer obvious relapses after the age of eleven or twelve years. Thus a condition of resistance seems to begin to develop about the age of puberty. But the period of greatest incidence of new cases during the first few years of school life is worthy of emphasis. Is it the result of intimate contact like that

seen in measles, or is it due to an age-linked hypersensitiveness? The experience of many observers teaches that the infection is progressing steadily in the hearts of many children while avoiding other organs. For example, Sutton[23] found in the Bellevue Hospital 18 per cent of 427 rheumatic children to have well-developed rheumatic carditis without a previous history of either polyarthritis or chorea.

An apparent precursory factor in a majority of cases is repeated infection in the respiratory tract, often in the form of tonsillitis, sinusitis, middle ear disease, or bronchitis. In our experience so frequent has been the occurrence of acute tonsillitis within from one to five weeks of an acute attack that we now date the duration of a given attack from the onset of tonsillitis. But more detailed investigation of the previous state of health of patients usually reveals an earlier history of repeated sore throats, otitis media, or of recurring or almost continuous sinusitis. Not infrequently closer questioning discloses mild joint or growing pains with these upper respiratory infections. Coates and Thomas,[24] Coates and Coombs,[25] and Vining,[26] all report the finding of small subcutaneous granules in a fairly high percentage of school children. Whether or not these are genuine rheumatic subcutaneous nodules is a moot point; but their alleged demonstration by serious students of the disease should stimulate renewed investigation, because extensive painless nodules have been frequently observed in children having no other symptoms of sufficient severity to incapacitate them.

Other conditions in many children preliminary to an acute attack are loss of weight, anorexia, and general signs of mild intoxication. To these Vining has applied the term "toxic debility," and found that many of his rheumatic youngsters had in addition a history of intestinal disturbance of sufficient severity to point to the intestinal tract as an area whence the infectious agent might be spread throughout the body. The greater liability of children of the poorer classes to suffer disorders of malnutrition or to be deprived of certain accessory food substances suggests that possibly these are elements leading to a higher incidence of the disease among such individuals compared with people living on a higher economic scale. Recent studies of rheumatic children in out-patient departments furnish additional support concerning the influence of nutrition, in that loss of weight has been found to be one of the most common precursors of a relapse.

Recurrences of symptoms sufficiently severe to be called true relapses are commonly observed in children year after year; but symptoms and signs too mild to attract much attention not infrequently occur between relapses. For example, Shapiro[27] has recently noted electrocardiographic evidence of active cardiac damage in at least 60 per cent of 119 school children following apparently complete recovery from an acute attack; and Levy and Turner[28] have recorded electrocardiographic abnormalities weeks and months before the onset of acute symp-

toms. Persistent low-grade leucocytosis, unexplained on grounds other than that of persisting rheumatic infection, is not infrequent. Several of our patients have observed recurring erythema marginatum for months without appreciating its significance until more incapacitating manifestations forced them to seek hospital care, and the continuance of this peculiar rash for weeks or months following subsidence of acute arthritis not infrequently is an index of continuing infection.

Not only are such pictures seen in children, in whom we have learned to expect repeated relapses, but a similar history is not rare in adults when sought with sufficient care. For example, a man, aged thirty-three years, in good circumstances gave a history of acute tonsillitis in 1929 followed by acute rheumatic polyarthritis, then by tonsillectomy. In the winter of 1930 he had sore throat followed by a similar polyarthritis. But more careful questioning revealed repeated pharyngitis for eight to ten years previously, several attacks of sinusitis and recurring pain in the neck and back of sufficient severity to make movements difficult. It does not appear unreasonable to suppose that during the previous years he was suffering from mild rheumatic infection which was not brought to acute intensity until his first attack of severe tonsillitis. Such histories are not rare.

That tonsillitis plays an important rôle in precipitating many acute attacks of rheumatic fever we can accept as fairly well established. Where both diseases are reportable, the peak of the curve of the former antedates that of the latter by about two weeks. Glover,[29] in presenting details concerning several concomitant epidemics of these two conditions, advances the theory that they are spread by droplet infection which must reach a certain intensity before the resulting diseases reach epidemic proportions. In one outbreak carefully studied, the carrier rate for meningococci and the incidence of cerebrospinal meningitis and of rheumatic fever ran parallel; and this suggests that similar influences were at play in causing an increase in all three conditions. With a diminution in crowding there was a disappearance of both diseases, and with renewed crowding there was a return of an equal number of each. While these appeared to be primary attacks of rheumatic fever, one would like information concerning the previous history of the rheumatic individuals. Such questions are raised by the study of epidemics among children with rheumatic heart disease or convalescent from rheumatic fever, such as reported by Boas and Schwartz,[30] and Hiller and Graef.[31] In the first epidemic reported by the former group there were four cases of bronchopneumonia accompanied by rheumatic carditis and one case of acute tonsillitis; in the second, although the precursory respiratory infection was not so marked, still acute rheumatic exacerbations developed in six boys in rapid succession. Among 19 nonrheumatic children in the same wards, none suffered from rheumatic fever, while in 22 previously rheumatic sub-

jects 11 developed acute rheumatic fever. In the epidemic reported by Hiller and Graef there were 43 children exposed, of whom 39 probably were previously rheumatic. Within five days of arrival at the camp there were twelve cases of upper respiratory infection, and within five weeks ten cases of polyarthritis, one of chorea, two of bronchopneumonia, one of acute bronchitis, and one of tonsillitis, pericarditis and pneumonia. Unfortunately the exact relationship of the upper respiratory infections to polyarthritis in each case was not recorded; nevertheless the high incidence of acute exacerbations of the disease in previously rheumatic children is worthy of emphasis, as is also the occurrence of severe pulmonary infection.

Scarlet fever is another disease intimately associated both with first attacks and with relapses of rheumatic fever. Some clinicians state that this disease in previously rheumatic children is practically always followed by acute manifestations of rheumatic fever. This suggests the possibility of comparable influences in all of the above mentioned epidemics, namely upper respiratory infection.

I realize fully the possibility of at least two interpretations of the phenomena described: (1) That rheumatic fever may be due to an unknown virus which may long lie latent in the body, and be incited to renewed activity because of the depressing influence of the acute respiratory infection; (2) on the other hand, it is possible that repeated and persisting low-grade infections induce or are accompanied by tissue changes too mild to be dignified by the name rheumatic fever, and that only with a stormy acute infection such as tonsillitis, or with invasion of the pulmonary tract by streptococci are the accompanying morbid processes raised above the clinical horizon. In either case the conditions existing prior to the attack of acute rheumatic fever are worthy of more detailed study than they usually receive.

To illustrate this point let us consider another group in which a contagious element may exist—the family. Since St. Lawrence's[32] report eight years ago showing the incidence of multiple cases of rheumatice fever in a group of families to be as high as that of tuberculosis, there have been several confirmatory studies. It now appears that in a rheumatic family with one case the probability of occurrence of a second case is three or four times as great as in a family previously free from the disease. Although the various factors favoring the development of rheumatic fever may be almost as difficult of analysis within a family as in any other group, the family as a unit offers a promising field for investigation. For example, several years ago we learned that the mother of one of our rheumatic children frequently had sore throats within a short time of the appearance of relapses in the child. Following the removal of badly diseased tonsils in the mother her sore throat ceased, and since then the child has been free from

recurrences. Last winter a boy was admitted to the hospital with the following recent history of acute infections in himself, his mother, and sister:

First day, onset of grippe in patient and sister.

Second day, patient better; sister developed rash.

Eighth day, mother developed grippe with severe pain in back; sister recovered and lost rash.

Twelfth day, mother recovered.

Fourteenth day, patient developed fever and beginning polyarthritis.

Sixteenth day, patient had evidence of severe myocarditis.

Nineteenth day, patient had signs of pericarditis.

Such a history of contagion reminds one of the concomitant respiratory infections in the epidemics mentioned above and suggests the possibility of atypical nondiagnostic manifestations in the sister and mother. Indeed, a correlation of all of the illnesses of the members of fifteen rheumatic families by Paul and Salinger[33] has already yielded important data along these lines. They have shown that both primary and secondary attacks of rheumatic fever in certain members of a family have been accompanied by the simultaneous appearance of recognizable rheumatic fever in other members of the family, and not infrequently by the appearance of such nonspecific affections as sore throat, bronchitis, bronchopneumonia and skin rashes. They found in addition that the disease spread more frequently to the children under twelve years of age than to the older children and adults. Another striking feature among these families was the frequency with which so-called nonspecific respiratory infections occurred before the appearance of characteristic rheumatic fever. If an extension of this type of investigation yields similar data, we shall be in a position to formulate preventive measures not heretofore applied. Indeed, the information already available from the several reports above reviewed together with those of Andrieu,[34] Grenet,[35] Irvine-Jones[36] and others suggests strongly the communicable nature of the infection. The time when health authorities will recognize this feature of the disease and attempt to assemble data compiled from compulsory notification may be nearer than we can now foresee. The numerical and economic importance of the problem far outweighs that of poliomyelitis, encephalitis, leprosy, and many other reportable diseases.

One more feature deserves attention: the hypersensitiveness of patients with rheumatic fever to streptococcal products, which has been found by most observers to be higher than in any other disease. One must admit that such hypersensitiveness is found in many nonrheumatic persons; hence these skin tests have not diagnostic specificity. But it has offered a possible explanation of certain peculiarities of the disease.[37] Mackenzie and Hanger,[38] Kaiser[39] and Ando[40] have all shown this type of hypersensitiveness to be rare or absent in infancy and to

increase in relative frequency with each half decade up to the period of adult life. In Duckett Jones's[41] experience over 95 per cent of rheumatic children gave positive reactions to a filtrate of a single strain of indifferent streptococci. Derick and Fulton[42] have recently found skin hypersensitivity to hemolytic streptococcal nucleoproteins in 88 per cent of rheumatic children between six and ten years of age compared with only 12 per cent in nonrheumatic children, surely a most significant difference, when it is noted that 88 per cent of their entire group of rheumatic fever patients gave positive reactions. It thus seems that hypersensitiveness to streptococci which appears with advancing years in many individuals occurs much earlier in rheumatic fever patients. Probably the repeated respiratory infections already so frequently mentioned are factors in conditioning a high sensitivity to streptococci; and it does not seem improbable that the condition recognized as acute rheumatic fever is incited by intense, focal infections such as acute tonsillitis, or otitis media—both due to hemolytic streptococci—occurring in already somewhat hypersensitive bodies. On the other hand, it must be recognized that we do not know definitely whether the relationship between streptococcal hypersensitiveness and rheumatic fever is causal or merely concomitant. Its existence, however, gives us a definite point of attack,[43] for could we influence it in one direction or another we would have an index with which to judge the effect of certain therapeutic efforts.

SUMMARY

Rheumatic fever is one of the most important of diseases economically, not only because of its acute manifestations, but also because of its rôle in the production of between 30 and 40 per cent of chronic cardiac disease in the latitude of the North Atlantic States. Microscopic findings indicate it to be a widespread disease involving by preference mesenchymal structures or mesenchymal portions of parenchymatous organs. Physiological stress and strain appear to favor localization of its manifestations, although it may be locally active without giving rise to symptoms; and various vulnerable organs may be either simultaneously or independently involved.

A number of factors appear to have causative relationships. Climatic conditions such as exist in temperate zones in winter favor its development; while sunny dry summers and tropical weather inhibit or prevent its evolution. Among the poorer classes it is from fifteen to twenty times more prevalent than in persons better housed and fed. Malnutrition and mild toxic states are frequent precursors of characteristic attacks. Most patients, both children and adults, give a history of repeated nonspecific infections of the respiratory tract, tonsils, sinuses, or middle ear, extending over several years, before a typical attack of rheumatic fever is ushered in by a severe focal infection.

Persons in intimate contact with patients during acute outbursts of rheumatic fever not infrequently suffer simultaneously from upper respiratory infections, or from typical rheumatic fever; hence there seems to be a distinct communicable factor favoring its spread. Because chronicity and relapses are so frequent, and crippling cardiac damage is of such gradual evolution, and finally because laboratory tests often reveal activity in periods between attacks, it seems justifiable to consider the infection to be characterized by long periods of preparation or sensitization of the tissues, the result of repeated mild infection before a more intense focal infection sets off the violent explosion recognized as acute rheumatic fever. Similar mild infections, moreover, apparently favor the continuation of true rheumatic activity in viscera already involved. It seems logical, therefore, to regard these preparatory periods and mild chronic infections between acute outbreaks as essential parts of the morbid process; hence our therapeutic and prophylactic efforts should be directed against them as well as against the more acute manifestations of the disease.

Note at time of correction of proof: While this article was in press the monograph[44] of Coburn appeared which presents much valuable additional evidence concerning the chronic and contagious nature of rheumatic fever; its geographic distribution; the high degree of cutaneous sensitivity of rheumatic fever patients to hemolytic streptococcal nucleoprotein; and finally a striking parallelism between an increase of hemolytic streptococci in the upper respiratory tract and relapses in patients with the disease. He apparently wishes to designate the malady as the "rheumatic state" and only recognizes "rheumatic fever" when it is diagnostically clear cut.

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THE INTERPRETATION OF THE INITIAL DEFLECTIONS OF THE VENTRICULAR COMPLEX OF THE ELECTROCARDIOGRAM*

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INTRODUCTION

BARKER, Macleod and Alexander[1] have recently reported a series of observations upon the exposed human heart which strongly suggests that the clinical electrocardiograms currently ascribed to right bundle-branch block are, in reality, due to left bundle-branch block and *vice versa*. This conclusion, if accepted, involves something more than a mere change in electrocardiographic nomenclature; it is in conflict with the prevailing views regarding the origin of the initial ventricular deflections of the normal electrocardiogram and of those curves now attributed to preponderant hypertrophy of the one or the other ventricle. These views, long held and almost universally accepted, were originally advanced by Lewis.[2] Based by him upon his careful and exhaustive study of the excitatory process in the vertebrate heart, they rest upon a foundation which has always seemed secure from both the experimental and the theoretical standpoint.

Nevertheless it seems to us impossible to reconcile these views with the observations upon the human heart referred to, and we therefore propose to reexamine the observations made by Lewis and his associates in order to determine whether they may justifiably be interpreted in such a manner as to avoid this conflict.

A FUNDAMENTAL HYPOTHESIS

We may point out at the outset that we are in complete agreement with Lewis regarding the significance of the electrical axis, determined by means of Einthoven's triangle. We believe, as does he, that at any given instant this axis points in the direction in which, on the average, the excitatory process is at that moment spreading. In other words, the direction of the electric force produced by the excitation of any muscle unit is determined by the direction in which that unit is activated, and not at all, as was at one time thought, by its position in space with respect to the muscle mass, as a whole, of which it is a part.

This hypothesis was advanced by Lewis in order to explain his experimental results; it was discussed with Einthoven and accepted by him,[3] and it is in accord with the results obtained by Craib[4] in his experiments upon isolated strips of cardiac muscle. Recently, we have

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shown that it is supported also by the form of the curves obtained by leading directly from the mammalian auricle, and that it can be derived on theoretical grounds from the so-called membrane theory.[5] It may be pointed out here that the acceptance of this hypothesis involves the acceptance of certain corollaries derived from it.

If it is true that the direction of the electrical axis is determined by the direction in which the excitation process is advancing or, in other words, by the position of the muscle which has just completed, or is just completing, the transition from the resting to the active state with respect to the muscle which is just beginning, or is just about to begin, this transition, it must necessarily follow:

1. That the position, with respect to the resting muscle as a whole and likewise with respect to the active muscle as a whole, of the muscle fibers undergoing activation is immaterial.
2. That muscle fibers or units in the resting state produce no electric currents.
3. That muscle fibers or units which are fully active produce no electric currents.
4. That all of the electric currents associated with the activation of heart muscle arise within fibers or units which are in a state of transition from the resting to the active state.
5. That the electric forces which accompany the wave of excitation are perpendicular to the wave front; that is to say, normal to the imaginary surface which separates active from inactive muscle and that these forces originate within the immediate neighborhood of this surface.

CURRENT INTERPRETATION OF HUMAN BRANCH-BLOCK CURVES UNSATISFACTORY

The interpretation of the initial phases of human branch-block curves advanced by Lewis and at present generally accepted is based to a considerable extent upon the hypothesis under consideration. Lewis[2] carefully measured and charted the early phases of human curves of the type ascribed to right branch block. He then calculated the electrical axis at intervals of 0.005 second over a period of 0.07 second, or approximately one-half the QRS-interval. It was found that the electrical axis, which at first pointed downward and slightly to the right, gradually rotated in a counter-clockwise direction through an angle of about 150 degrees. A similar analysis of clinical curves ascribed to left branch-block was carried out, and in this case the electrical axis, which at first pointed downward and slightly to the left, rotated in a clockwise direction through an angle of similar magnitude.

Granting the correctness of the hypothesis upon which it rests, this method of analysis gives the average direction at any instant and the variations in the average direction in which the excitatory process was spreading over the ventricular muscle during the period in which the

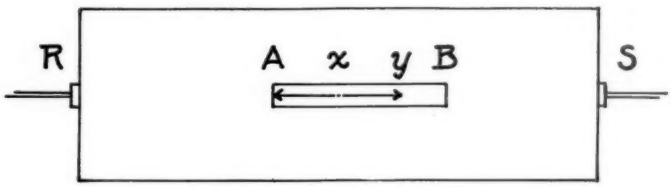
curves analyzed were inscribed. We do not question this conclusion. The use which Lewis made of it depended, however, upon a comparison of the electrical axis at a given instant with an estimate of the average direction in which the excitatory process was spreading at the same moment. This estimate was based upon anatomical considerations and upon the order of ventricular activation, which was determined in detail in the dog and assumed to be similar in man. To estimate the average direction in which the excitatory process is spreading at a given instant is, however, a matter of some difficulty, for during the greater part of the QRS-interval it is advancing in many different directions at the same time. The factors that must be taken into consideration are numerous and complex in kind, and it is quite possible, in many cases, that the estimate may be approximately correct although the ideas upon which it is based are erroneous. In the case of the clinical curves ascribed to left branch block, Lewis came to the conclusion that the electrical axis rotated in a clockwise manner because of the activation in succession of the right side of the septum from right to left, the apical muscle of the right ventricle from above downward, and the lateral wall of the right ventricle from within outward or from left to right.

In this instance the behavior of the electrical axis seems to be entirely in accord with the estimated variations from instant to instant in the average direction in which the excitation process spreads over the right ventricle, and strongly to support the view that curves of the type in question are the result of left branch block. If, however, the same method of analysis is applied to that portion of these curves which is written during the last half of the QRS-interval, and which must be attributed to the activation of the muscle of the left ventricle, the position of the electrical axis brings us to the surprising conclusion that the average direction, in which the excitatory process spreads over the muscle of this chamber, is from left to right and from below upward. Inasmuch as the excitation wave in left branch block must cross the septum from right to left and must pass through the lateral wall of the left ventricle in the same general direction, it is obviously improbable, if not impossible, that this conclusion can be correct. The only considerable mass of muscle that is activated from left to right is the comparatively thin wall of the right ventricle; the thick septum and the thick lateral wall of the left ventricle must, on the average, be activated from right to left. It is difficult, therefore, to believe that throughout by far the greater part of the QRS-interval the average direction in which the excitation process is spreading is from left to right as the prevailing conception of left branch block requires.

This difficulty was encountered some years ago by Wilson and Herrmann[6] when they attempted to determine the theoretical form of the true dextrocardiogram and levocardiogram, but it has escaped further

attention. Cardiologists have apparently avoided the dilemma by assuming, consciously or unconsciously, that the electric forces produced by the activation of the lateral wall of the right ventricle persist so long as this muscle remains in the active state, or at least until they are neutralized by the forces produced by the activation of the left ventricle. This method of avoiding the difficulty, however, involves the simultaneous acceptance of two theories which cannot be reconciled. It is impossible to hold that the electrical axis at any instant points in the direction in which, on the average, the excitatory process is spreading, and to believe at the same time that cardiac muscle continues to produce electric currents after it is fully active. The two theories which Lewis[7] has called the "*theory of limited potential differences*" and the "*theory of distributed potential differences*" are incompatible with one another and cannot be successfully combined.

It is apparent, therefore, that the current interpretation of human branch-block curves is not entirely satisfactory. The difficulty which



$$Ax = xy$$
$$Rx = xS$$

Fig. 1.

we have referred to is fairly obvious. There are a number of others which are less easy to make evident. The nature of these difficulties and the manner in which they may be avoided can best be brought out by a discussion of some simple theoretical experiments.

ANALYSIS OF THE ELECTRICAL EFFECTS PRODUCED BY A MUSCLE STRIP

Let us suppose that AB (Fig. 1) is a short narrow strip of uninjured cardiac muscle immersed in a large quantity of Ringer's solution, and that two nonpolarizable electrodes, in contact with this solution at R and S, are attached to the right- and left-hand terminals of the string galvanometer respectively. If the muscle is stimulated at x, a point equidistant from R and S, the excitation process set up will spread to the right and to the left and will reach A and y, which are equidistant from x simultaneously. During this period the currents produced by the spread of the excitation process to the right (toward A) will be exactly neutralized by the currents produced by the spread of the excitation process to the left and the galvanometer string will remain

in the zero position. The currents produced by the activation of that part of the muscle lying between y and B will not, however, be opposed and will produce an upward deflection indicating relative negativity of R, with respect to S. During the inscription of this deflection the electrical axis will at all times point from the point of stimulation toward the center of the muscle. The absence of any deflection in the lead RS, during the period when the excitation process is spreading from x to A and to y, is dependent upon the assumption that R and S are equidistant from x. Suppose that instead of this indirect lead, a direct lead is employed in which the right-hand electrode at R is placed in contact with the end of the muscle at A and the left-hand electrode is allowed to remain at S. If S is distant from the muscle, the potential variations of the exploring electrode at A will be so much greater than those taking place at the electrode at S that the latter may be neglected. Inasmuch as the muscle units lying between x and A are much closer to the exploring electrode than the muscle units lying between x and y the activation of the former will have a much greater effect upon the potential of this electrode than the latter. Consequently, the electrode at A will be relatively positive with respect to the electrode at S and the galvanometer will record a downward deflection during the period in which the excitatory process is spreading from x to A. This downward deflection will reach its apex at the instant when the excitatory process reaches A; that is to say, at the moment when the muscle at A begins to pass into the active state. The electrode at A will remain positive with respect to the electrode at S until the muscle at A is fully active. The former electrode can never become relatively negative with respect to the latter except as a result of the activation of muscle units lying between y and B. The beginning of the upstroke, or "intrinsic deflection," recorded at A signals the arrival of the excitation process at A; the point where this upstroke crosses the base line marks approximately the completion of the activation of the muscle at A; the remainder of the upstroke is written by the activation of muscle units lying between y and B. The upward deflection in the indirect lead RS must begin at the instant when the intrinsic deflection of the direct lead has its onset, for it is at this moment that the currents produced by the spread of the excitatory process toward A begin to decline and become unequal to the opposed currents produced by the spread of the excitatory process toward B.

A CRITICISM OF THE CURRENT INTERPRETATION OF THE CANINE LEVOCARDIOGRAM

In the experimental studies carried out by Lewis and Rothschild[8] the exploring electrode was placed upon the ventricular surface and the indifferent electrode upon the chest wall. The onset of the "intrinsic deflection" recorded in this manner must indicate that the excitatory

process, which travels from within outward, has reached the epicardial surface beneath the exploring electrode, and that the activation of the subjacent section of the ventricular wall has been completed, or at least that it will be completed within 0.01 second or less. The electrical effects produced by this portion of the ventricular wall must begin when the excitatory process starts to spread outward from the endocardial surface; they must end when it reaches the epicardial surface, or at any rate when the subepicardial muscle becomes fully active.

In discussing the discordant levocardiograms which he obtained in a small percentage of dogs, Lewis[2] stated that the direction of the electrical axis in the coronal plane was in agreement with representative readings, indicating the temporal orientation of the "intrinsic deflections" from the surface of the left ventricle with respect to R of Lead II. The figures which illustrate this statement[2] (Figs. 4 and 5, pp. 260 and 262) show, that about 0.01 second after "intrinsic deflections" are recorded over a given section of the free wall of the left ventricle, the electrical axis points in the direction in which this portion of the wall is activated. It is difficult to understand why the electrical axis should point in the direction in which the excitatory process spreads over a given mass of muscle at a time when the activation of this muscle has been practically, if not entirely, completed. There is still another difficulty. While the excitatory process is spreading through the lateral wall of the left ventricle, it must also be spreading through the septal wall, which is equally thick if not thicker. The electrical effects produced by the one group of fibers must be almost directly opposed by those which are produced by the activation of the other. There is little reason to suppose that these opposed electric forces differ materially in magnitude. It would seem, therefore, that the direction in which the lateral wall of the left ventricle is activated can hardly determine the position of the electrical axis until the activation of the septal muscle is complete. But when the excitatory process has completed its spread through the septum, activation of the right ventricle is already beginning and we are no longer dealing with purely left ventricular effects. The interpretation of the human dextrocardiogram and levocardiogram offered by Lewis[2] is open to the same objections.

The analysis of the experimental curves referred to is open to criticism on still other grounds. Surface readings taken from dogs in which the form of the levocardiogram was not investigated cannot justifiably be compared with the electrical axis calculated from a levocardiogram of the discordant type which is known to be exceptional.

We have pointed out that it is often difficult to form an accurate estimate of the average direction in which the excitation process is spreading at a given instant, even when the order of ventricular excitation is known. Consequently, as we have indicated in the discussion above, there is frequently an advantage in considering the direction of

spread, not at a given instant, but during a given period, or during the QRS-interval as a whole. There are, however, a number of considerations upon which an estimate of the kind first mentioned may be based.

ELECTRICAL EFFECTS PRODUCED BY A SPHERE OF EXCITABLE TISSUE

Suppose that the heart were a sphere of homogeneous excitable tissue and that the natural impulses were formed at its center. The excitation process would then spread radially outward as indicated in Fig. 2. Throughout the period of excitation the mass of fully active muscle must in that case form a perfect sphere completely enclosed by muscle in the resting state. Consequently, the imaginary surface separating active from resting muscle must also be spherical and must be com-

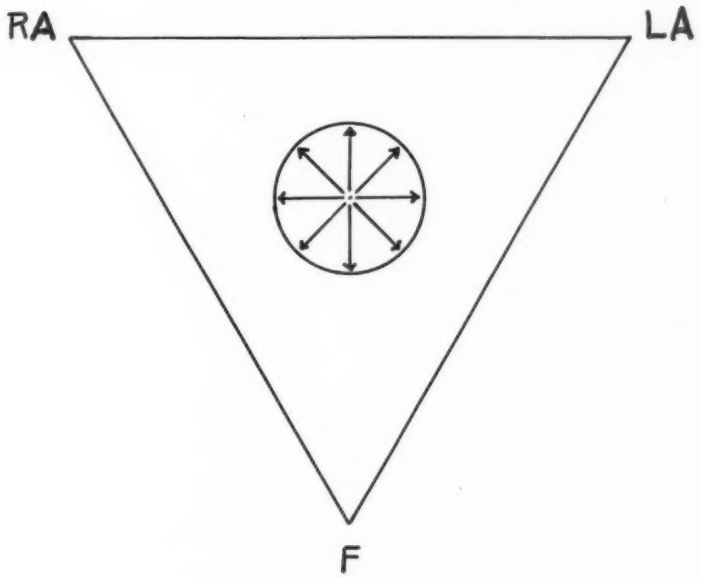


Fig. 2.

pletely closed. For every muscle unit undergoing activation in one direction at a given instant there must be another muscle unit undergoing activation in exactly the opposite direction; and the electrical effects produced by the one must be completely neutralized by the effects produced by the other. At no time could unbalanced or unopposed forces exist, and at no time could there be a deflection in any of the three standard leads.

Suppose, however, that this theoretical heart be stimulated artificially at some point between the center and the outer surface. The active mass of muscle and the surface separating it from inactive muscle must clearly be spherical until the excitation process reaches the surface at the point nearest the point of stimulation. No unbalanced forces and no deflections in any standard lead can occur previous to this time. As

soon as the excitation process reaches the surface of the sphere, however, unbalanced forces must occur, and obviously the magnitude of these forces must depend upon the number of muscle units producing unopposed electrical effects, and consequently upon the area of the opening or break in the surface separating active from resting muscle. The muscle units "visible" through this opening from a distant point, supposing the active muscle to be transparent, the resting muscle opaque, have no opposition, at least in so far as effects parallel to the line of vision are concerned.

It is not difficult to see that the principles underlying these statements apply in simple cases, such as the one discussed, which possess a high degree of symmetry. It is less easy to see that they are applicable also to cases of a complicated kind.

A METHOD OF ESTIMATING THE RESULTANT ELECTRICAL FORCE

If it is agreed that the electric forces which accompany the excitation wave are at all times perpendicular to the wave front, that is to say, normal to the imaginary surface which separates the active from the resting muscle, the electric field produced by these forces must be of the same character as that produced by a membrane polarized in a direction normal to its surface. From the mathematical standpoint the problem of determining the distribution of the electric currents is exactly the same in both cases. Furthermore, if we accept the membrane theory, the electric field in the first case is in fact the electric field of the polarized membranes of the fibers undergoing activation.

We have discussed the nature of the electric field surrounding a membrane polarized in the manner specified in another place.[5] We have shown that, when the medium in which the membrane lies is infinite in extent, the potential V of any point P within the field is determined by the following equation:

$$V = \phi\omega$$

where ϕ is a constant, which may be defined as the electrical moment per unit surface of the membrane, and ω is the solid angle subtended by the membrane at P. The solid angle is defined and measured by the area cut out upon a spherical surface of unit radius, inscribed about P, by the cone formed by drawing a line from P to every point upon the boundary of the membrane. It may, for convenience, be considered negative or positive according as an observer looking through this cone sees the negative or the positive side of the membrane, for the sign of V is determined by this test. The same equation must also define the electric field surrounding the surface which separates active from resting muscle, the side of this surface adjacent to the resting muscle being considered positive and that adjacent to the active muscle, negative. The potential at any point within this field is therefore proportional to the

solid angle subtended by this surface at that point. It is true that if the medium is not infinite the equation given is not accurate; but, as we have pointed out elsewhere the error introduced by considering the body as if it were an infinite medium is for many purposes of little consequence. The equilateral triangle of Einthoven, upon which the calculation of the electrical axis is based, is founded upon the assumption that the apices of the triangle are distant and equidistant from all parts of the heart.[9] If this assumption is made, the potentials of the apices of the triangle appear in fact to be strictly proportional to the solid angles subtended by the surface referred to at these points,[5] although in this case the constant ϕ may no longer be equal to the electrical moment per unit surface, but a multiple of it. The assumption that

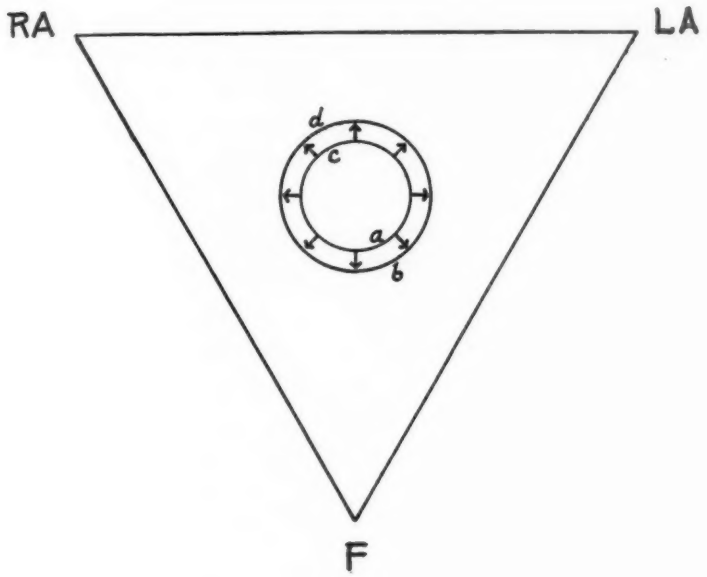


Fig. 3.

the apices of Einthoven's triangle are, for practical purposes, distant and equidistant from the heart is equivalent to the assumption that the heart is at the center of a spherical medium of large radius upon the surface of which the apices of the triangle lie. In that case the electrical axis may be defined as the vector drawn from the point on this spherical surface at which the solid angle subtended by the surface specified has its greatest negative to the point where it has its greatest positive value.

If the surface which separates active from resting muscle is completely closed, the solid angle subtended by it at all outside points must be zero. This is readily seen, for if such a surface is divided into two portions by means of an optional plane, the two surfaces thus formed will have the same edges or boundaries and the solid angles subtended

by them at any outside point must be equal in absolute magnitude, but unlike in sign. The sum of these two angles and consequently the potential of all points outside the surface under consideration must, therefore, be zero. So long as this surface remains closed no deflection can occur in any lead, direct or indirect. It is also clear that if there is a single opening in this surface, otherwise closed, the boundaries of the surface and of the opening are the same, and the solid angle subtended at any point by the one must be equal in absolute magnitude to the solid angle subtended by the other. If more than one opening is present, the sum of the solid angles subtended by all of them, each angle being given its proper sign, must be equal to the solid angle subtended by the surface. In estimating the potential at an outside point it does not matter, therefore, whether we consider the surface itself or the openings in it. Since the solid angle is determined by the boundaries of the surface alone, the configuration of the latter is immaterial.

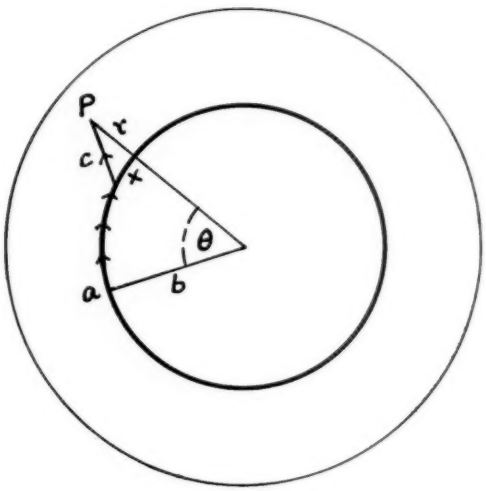


Fig. 4.

NORMAL AND TANGENTIAL COMPONENTS

Consider now a theoretical heart, which, instead of being a solid sphere, is a spherical shell of homogeneous excitable tissue, and suppose that all points on the inner surface of the shell are activated simultaneously. The excitation process will then spread through the wall along lines radiating outward from the center (Fig. 3), and again no deflections will occur, either in indirect or in direct leads, at any time during the period of excitation. We have assumed that all points on the inner surface of the shell are activated simultaneously; we can suppose that this result is brought about by a thin sub-endocardial layer of special tissue, which conducts the excitation process with infinite speed.

Suppose, however, that this thin layer conducts the excitation process with a speed which is only five times as great as the speed with which this process is transmitted by the tissues which enclose it. In that case the muscle units of the shell will not be activated in a direction normal to the surface. It is desirable to know the approximate direction in which these units will be activated. Let us suppose that the point of stimulation is a (Fig. 4); that b is the radius of the inner sphere and that P is any point of the shell, and r the distance of P from its inner surface. In reaching P the excitation process will obviously follow a course somewhat like that indicated by arrows; this course consists of two parts, $b\theta - x$ which represents the path through the lining layer, and c which represents the path through the ordinary tissue. Since the speed of transmission is five times as great along the first part of the path as the second the time t required by the excitation to reach P may be represented by the equation

$$t = \frac{b\theta - x}{5} + c$$

If the thickness of the shell is small in comparison with b, the angle subtended by the arc x must be small, and the triangular area bounded by r, c and x may be considered practically equivalent to a right triangle. Consequently c is approximately equal to $\sqrt{x^2 + r^2}$. Our equation then becomes

$$t = \frac{b\theta - x}{5} + \sqrt{x^2 + r^2}$$

Since the excitation process will reach P by the path which is least time-consuming we must determine the value of x when t reaches its minimum value. This may be done by differentiating t with respect to x and equating the derivative to zero. We have $\frac{dt}{dx} = -\frac{1}{5} + \frac{x}{\sqrt{x^2 + r^2}}$ and when $\frac{dt}{dx}$ becomes zero $x = \pm\frac{r}{\sqrt{24}}$. In other words x is approximately one-fifth of the distance of P from the inner surface of the shell. If the electrical force produced by the activation of any muscle unit of the shell is resolved into two components, one normal and the other tangential to the inner surface of the shell, the normal component will be approximately five times as great as the tangential.

ELECTRICAL EFFECTS PRODUCED BY A SIMPLE SHELL OF MUSCLE

Let us now return to the theoretical heart illustrated in Fig. 3. We have assumed that the inner surface of the shell is lined by a thin layer of special tissue which conducts the excitatory process five times as rapidly as the outer layers. The excitatory process set up by a stimulus applied at a will spread rapidly over the inner surface and slowly outward through the wall. The activation of each muscle unit will produce

an electric force which may be considered the vectorial sum of a normal and a tangential component, the former five times as great in magnitude as the latter. The electrical axis produced by the tangential components, considering these alone, will at all times point from the point of stimulation toward the center of the shell, or from *a* toward *d*, the point at which the excitatory process is ultimately extinguished.

The electrical axis produced by the normal components considered alone, will at first point from *a* toward *b*, or, from the center toward the point of stimulation. If we suppose that the relation between the thickness of the shell and the radius of its inner surface is such that the excitation process reaches *c* before it reaches *b* the electrical axis produced by these components will maintain this position until the excitation wave has reached the former point. During the latter part of the period of excitation the electrical axis will point from the point of stimulation toward the center, or toward *d* the point of extinction. In Lead II, which is parallel to the line *ac*, the normal components will therefore produce an upright followed by an inverted deflection and since the sum of all the normal components must be zero, if they all occurred at the same time, these deflections must be alike in amplitude and in duration; that is to say, one must be, in all respects, the inverse of the other.

Since the tangential components tend at all times to produce a deflection downward they must decrease the amplitude of the upward deflection and increase the amplitude of the downward deflection produced by the normal components. The actual curve recorded must therefore consist of a positive deflection followed by a larger negative deflection. If the stimulus be applied at *c* instead of at *a* the resulting curve must be in all respects reversed. If two stimuli be applied simultaneously, one at *a* and the other at *c* no deflections at all could occur in any of the three standard leads.

If, as we have assumed, the excitatory process reaches *c* before it reaches *b* there will be a short period during which the surface separating active and resting muscle is completely closed. During this period there will be no deflection in any lead; consequently the positive and negative waves will be separated by a short iso-electric period, which will begin when the excitation process reaches *c* and will end when it reaches *b*. If the thickness of the shell is gradually reduced this iso-electric period will become shorter; it will disappear when the thickness of the shell is reduced to a point which permits the excitation process to reach *c* and *b* simultaneously. A further reduction in the thickness of the shell will cause the end of the positive and the beginning of the negative deflection to fuse, algebraic summation taking place as the components responsible for these portions of the two curves become simultaneous.

ELECTRICAL EFFECTS PRODUCED BY A COMPLICATED SHELL

The simple conditions depicted in Fig. 3 may be made more complicated in a variety of ways. We may suppose, for instance, that the two spherical surfaces which bound the shell are eccentric so that in the neighborhood of *a* the wall is two or three times as thick as it is in the vicinity of *c*. It is clear that the normal and tangential components of the electrical forces produced by the activation of the thickest portion of the wall of such a shell, in comparison with those produced by the activation of the thinnest portion, will not be greater in magnitude at any given instant, but only in duration; and that the difference in this respect will be proportional to the difference in thickness. If all

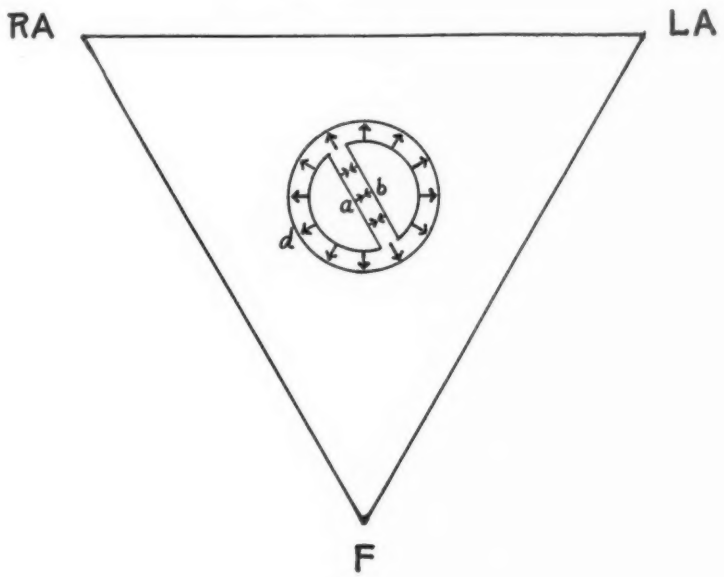


Fig. 5.

points on the inner surface are activated at the same instant there can be no deflection until the excitation process reaches the outer surface at the point where the wall is thinnest. It may be observed that the position and magnitude of the vector which represents the sum of all the tangential components is determined to a very large extent by the point of stimulation, whereas the vector which represents the sum of the normal components is determined by the distribution of the muscle of the shell wall. If the electrical forces produced are considered in their entirety, there is a close resemblance between the effect produced by shifting the point of stimulation in one direction and that produced by shifting the center of mass in the opposite direction.

We may also complicate the simple shell of Fig. 3 by introducing a septum as in Fig. 5. If all the points on the inner surface of this

double shell are activated at the same instant the course of the excitation process will be that indicated by arrows, and, since the electrical forces produced will be exactly balanced, there will be no deflection in any of the three standard leads during the period of excitation. If a stimulus is applied at *a* on the septal wall of the right ventricle of the shell, the electrical effect produced will be determined by the comparative thickness of the septum and the free wall of this chamber. If the excitation process arrives at *b* on the left side of the septum before it reaches *d* there will be a brief period during which the electrical axis points to the right and downward; but if the opposite is the case the electrical axis must at all times point to the left and upward. In either case, during the last half, approximately, of the period of excitation the electrical axis must point in the latter direction.

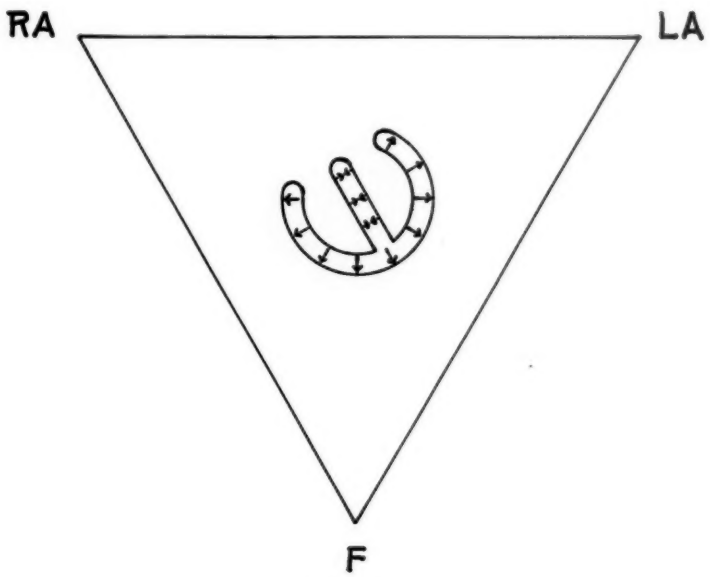


Fig. 6.

Finally, let us consider the theoretical conditions illustrated in Fig. 6. Here a cap has been removed from the shell so that the sum of all of the normal components is no longer zero. Consider that the general course of the excitation process over this structure is from within outward. If the excitation wave reaches all points on the inner surface before it reaches any point on the outer surface, there must be a period during which the solid angle subtended at any point by the surface which separates active from resting muscle is equivalent, or approximately equivalent, to that subtended at the same point by the openings in the shell at its base. It is clear that the solid angle subtended by these openings must be negative and large at *RA*, positive and large at *F*, and, as the figure has been drawn, positive and small at *LA*.

The electrical axis during the period referred to will, therefore, be nearly parallel to Lead II. If we draw a line from any apex of the triangle through every point upon the boundary of the surface which separates active and resting muscle, the potential of that apex at that moment is completely determined by the excitation of the muscle which lies within the cone or cones so formed. The sum of the effects produced by all other muscle is zero.

We have discussed these theoretical experiments and conditions at some length in order that the reader might have a clear understanding of the principles upon which, so we believe, the interpretation of the

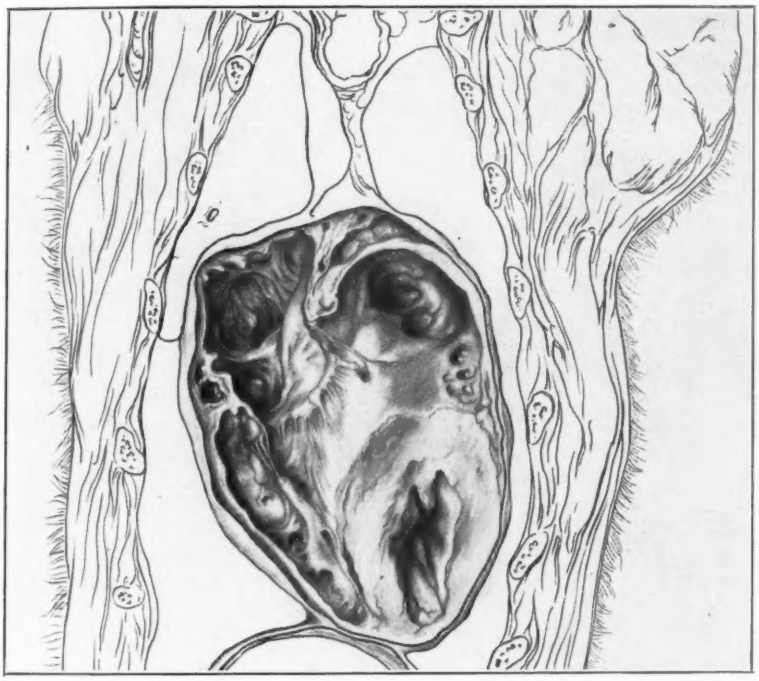


Fig. 7.—Frontal section of a dog's heart, well toward the ventral surface.

initial phases of the ventricular complex of the electrocardiogram must be based. We may now proceed to a consideration of the heart itself.

THE DEXTROCARDIOGRAM

We may first direct our attention to the right ventricle. Since the septum must obviously play a prominent rôle in determining the character of the dextrocardiogram, its position with respect to the three standard leads, and the direction in which it is activated are matters of importance. We have, therefore, prepared accurate drawings of the heart of the dog and of man sectioned in the frontal plane (Figs. 7, 8, 9, 10). Since the septum is not perpendicular to this plane, two

cuts were made in order to show the position of the more ventral (Figs. 7, 9) as well as of the more dorsal (Figs. 8, 10) portions of this structure. We may call attention here, to certain differences between the canine and the human heart.

In both dog and man the right ventricle lies on the right and ventral side of the left; in the former the right ventricle lies more above (Figs. 9, 10) the left (on its cephalic side); in the latter, more below it (Figs. 7, 8). As seen in coronal section the septum of the human heart is nearly parallel to that side of Einthoven's triangle which represents Lead II (Figs. 9, 10). The dorsal part of the dog's

Fig. 8.—Frontal section of a dog's heart, more toward the dorsal surface.

septum is nearly vertical (Fig. 8); its ventral part is curved and may be described as convex upward and to the right (Fig. 7). The normal components produced by the activation of the septal wall of the right ventricle must tend to produce an electrical axis which in the dog points to the left and downward, in man to the left and upward. Our knowledge of the order in which the subendocardial muscle on the right side of the septum is activated is too meagre to permit an accurate estimate of the direction of the tangential components.

The observations of Lewis and Rothschild[8] show that except for the conus region and the middle and upper portions of the septum, the entire endocardial surface of the dog's right ventricle is activated before the inscription of *R* in Lead II begins, or immediately thereafter.

Even at this time the excitation process has already reached the epicardial surface in the central region. In the imaginary surface which separates active and resting muscle there are at this period two openings; the electrical effects produced by those portions of the ventricular wall which lie opposite these openings, and these electrical effects alone, are unopposed. At the base of the ventricle, there is an opening in the surface which surrounds the tricuspid orifice and the canal of the conus arteriosus. As the excitation process spreads over the upper septum and over the endocardial surface of the conus, this opening may be divided into two parts. There is a second opening in the central

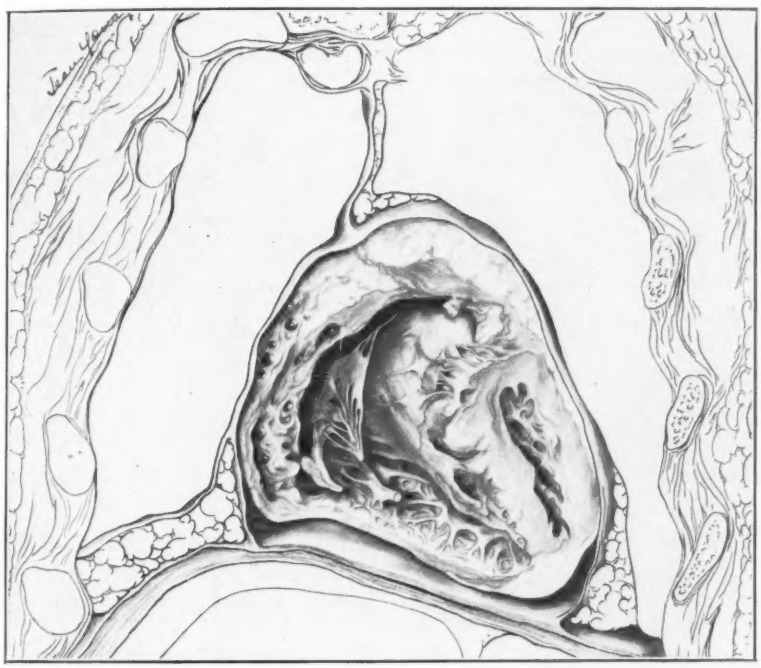


Fig. 9.—Frontal section of the human heart, well toward the ventral surface.

region, due to the arrival of the excitation process at the epicardial surface, which, although small at first, rapidly expands as the excitation process spreads over the outer surface of the lateral walls of the ventricle. The first opening must tend to produce an electrical axis pointing almost straight downward, perhaps slightly to the right at times; the second, an electrical axis pointing chiefly to the left, but with variations through a considerable angle. The resultant electrical axis must point downward and to the left. Apparently, the later and major portion of the canine dextrocardiogram must be attributed to electrical effects produced by the activation of the apical muscle and septal wall of the right ventricle. Except for the emphasis here laid upon the septal muscle, this view and that held by Lewis are not materially different.

The same principles may be applied to the interpretation of the human dextrocardiogram. We have pointed out that the position of the human heart with respect to the three standard leads differs materially from that of the dog. There is a further difference in the distribution of the subdivisions of the right branch of the His-bundle. Large and important strands of special tissue bridge the cavity of the dog's right ventricle. No similar conducting paths are found in man. It might be expected, therefore, that the excitation process would spread to the lateral wall of this chamber more quickly in the former than in the latter. The readings obtained by Barker, Macleod and Alexander[1] from the ventral surface of the exposed human heart are somewhat puzzling,

Fig. 10.—Frontal section of the human heart, more toward the posterior surface.

in that the earliest right ventricular points were not in the central region as in the dog but nearer to the base. These figures indicate, however, that the excitation process reaches the epicardial surface of the right ventricle somewhat later in man than in the dog. We need not attempt here to decide whether the cause of this difference is to be found in the distribution of the conducting tracts, the greater size of the heart, or in the thickness of the ventricular wall. It is clear that the excitation process spreads over the endocardial surface with great rapidity in man as in the dog. When the activation of the inner surface of the right ventricle has been completed, the surface which separates active from resting muscle must be open at the base. Because of the position of the human heart this opening will tend to produce an electrical axis which points downward and to the left in a direction

more or less perpendicular to the line of Lead III. When the excitation process reaches the epicardial surface, if it has not already done so, a second opening will appear on the lateral wall. Opposite this opening lies the septum producing electrical forces which, in terms of the electrical axis, point upward and to the left. As the opening increases in size, these effects will increase in magnitude. If we add these two vectors, the first pointing downward and to the left, the second upward and to the left, assuming that the latter, unlike the former, is small in the beginning but increases from instant to instant in magnitude, the resultant electrical axis will gradually rotate in a counter-clockwise direction.

We have pointed out that because it is difficult to estimate the average direction in which the excitation process is spreading at a given instant, there is an advantage in considering the average direction in which it spreads during the QRS-interval as a whole. Let us examine the effects produced by left branch block from this standpoint. The excitation process must spread through the septum from the right ventricle towards the left ventricle; it must spread over the left ventricle from its septal towards its lateral side; it must spread through the free wall of the left ventricle in the same general direction. Only the thin lateral wall of the right ventricle is activated in the opposite direction. In the dog the left ventricle lies on the left side of the right and below it and the average electrical axis, considering the period of excitation as a whole, must point to the left and downward. In man the left ventricle lies to the left of the right and above it, and the average electrical axis must point to the left and upward.

We believe that the clinical curves heretofore ascribed to right branch block are the result of left branch block, and consequently that the human curves which Lewis attributed to left ventricular effects and called levocardiograms were written by the muscle of the right ventricle and should have been labeled dextrocardiograms. We have indicated the manner in which, so we believe, the general outline of these curves and the counter-clockwise rotation of the electrical axis which takes place during their inscription are to be explained.

THE LEVOCARDIOGRAM

Lewis and Rothschild[8] found it difficult to obtain reliable readings from the endocardial surface of the left ventricle. The figures which they give indicate that in the dog the apex and the septal wall are activated before the beginning of *R* in Lead II, and that some points on the upper septum are very early.

When the activation ot the subendocardial muscle is completed, the surface which separates active from resting muscle must be open at the base where the ventricular wall is pierced by the mitral and aortic orifices. The forces produced by the apical muscle which lies opposite

these orifices are unopposed, and must tend to produce an electrical axis pointing almost straight downward. The left ventricular wall is thinnest at the apex and when the excitation process reaches the epicardial surface in this region a second opening will appear tending to produce an electrical axis pointing almost straight upward, or upward and to the right. The continued increase in the size of this opening as the excitation process reaches the epicardial surface over a larger and larger portion of the free wall must eventually enable it to more than overcome the effect of the opening at the base. The resultant electrical axis which at first points downward must therefore finally point upward and to the right.

In man because of the position of the heart, it would seem that the basal opening must tend to make the electrical axis point downward and to the left. As the activation of the lateral wall is completed septal forces pointing downward and to the right must become more and more effective. The resultant electrical axis must eventually point downward and to the right.

It may be pointed out that if the two vectors which represent the respective effects of the basal and the apical openings in the surface which separates active and resting muscle are directly or almost directly opposed to one another, the vector which represents their sum may suddenly undergo a reversal in direction if the relative magnitude of its components is gradually altered. If, on the other hand, the two vectors mentioned are not directly opposed the direction of the resultant will change more gradually; it will display a more or less uniform rotation.

Let us consider the direction in which the excitation process spreads over the ventricular muscle during the QRS-interval as a whole. In right branch block this process must spread through the septum from the left ventricle toward the right. The observations of Lewis and Rothschild show that it spreads over the right ventricle from its septal toward its lateral side. The free wall of the right ventricle must be activated in the same general direction.

Pointing in one direction we have the normal components of the electrical forces produced by the activation of the septum, and the tangential and normal components of the electric forces produced by the activation of the right ventricle. Pointing in the other direction we have only the effects produced by the lateral wall of the left ventricle. Clearly the mean electrical axis must point from the left ventricle towards the right. In the dog the right ventricle lies to the right of the left and above it, and the mean electrical axis should point to the right and upward. In man the right ventricle lies to the right of the left and below it, and the mean electrical axis should point to the right and downward.

We hope to return to this subject in a future communication in which we shall describe a method by means of which the mean electrical axis may be accurately calculated.

The foregoing considerations offer an explanation of the chief features of those human curves, which, according to our view, are produced by right branch block, and of the concordant levocardiograms which the majority of dogs display.

In a small percentage of dogs Lewis[2] obtained levocardiograms of the discordant type. During the inscription of these curves, which resemble the human curves now ascribed to right branch block, the electrical axis was found to rotate in a counter-clockwise direction. The views expressed by Lewis regarding the initial deflections of the human ventricular complex are based, to a very large extent, upon his interpretation of these discordant canine levocardiograms.

Lewis has tabulated[2, p. 257] his measurements of the bicardiogram and levocardiogram of twelve dogs. Two methods of interrupting conduction through the right branch of the His-bundle were employed. In one-half of the experiments this structure was cut by means of a knife thrust through the ventricular wall just below the pulmonary valves. In the remaining experiments a clamp was employed. The right branch lies on the right side of the septum relatively close to the ventral wall of the heart. When one jaw of the clamp presses upon it, the other jaw pressing upon the left surface of the septum can hardly fail to injure some of those conducting tracts which constitute what is usually referred to as the anterior subdivision of the left branch of the His-bundle. Lewis[2] mentions this possibility, but points out that unless the damage to the left branch is very extensive the order in which the muscle of the left ventricle is activated, in so far as this may be determined from the form of the axial electrocardiogram, is not altered.

Subsequent observations have shown, however, that transection of the anterior subdivision of the left branch may alter the form of the initial deflections of the electrocardiogram materially. Rothberger and Winterberg[10] found that when this structure was divided and the main stem of the right branch was also cut, the chief initial deflection of Lead I was usually upward. Wilson and Herrmann[6] have also published curves from an animal in which a levocardiogram of the concordant type became discordant when the anterior subdivision of the left branch was injured.

It is noteworthy that in the only two experiments in which the curves obtained by Lewis were *strikingly* discordant a clamp was used.[2, p. 257] In one of these curves R of Lead I reached a value of 2.6 millivolts (Dog H. V.), whereas R of the bicardiogram in the same lead measured only 1.3 millivolts. According to these figures the dextrocardiogram must show in Lead I a downward deflection of at least 1.3 millivolts

and must be of the discordant type. No one, so far as we know, has ever produced such a curve by cutting the left branch of the His-bundle.

We strongly suspect, therefore, that the discordant levocardiograms upon which Lewis lays so much stress, resulted from the use of a clamp which injured the anterior subdivision of the left branch of the His-bundle. We do not, of course, deny that in some animals, in which the deflections of Lead I are all comparatively small, the chief initial deflection in this lead is upward. Such curves cannot, however, be regarded as frankly discordant and do not resemble the human curves which are at present ascribed to right branch block.

Since the effects of cutting the anterior subdivision of the left branch upon the order of ventricular activation have not been studied it is not possible to offer a detailed explanation of the changes in the form of the levocardiogram which this procedure produces. It must be remembered that the plane of the septum is neither frontal nor sagittal but midway between the two. The conducting tracts which comprise the subdivision in question apparently distribute the excitation wave to the ventral portion of the septum and to the left anterior wall of the left ventricle, while the posterior division supplies the dorsal parts of the septum and the right posterior wall of this chamber. If the former tract is cut, the excitation process must spread from the dorsal margin of the septum toward the ventral margin, and consequently the tangential components of the electric forces produced by the activation of the septal muscle must point from right to left. The tangential components arising in the free wall must also be modified and must point in the same general direction. It is clear that whenever a conducting tract is blocked the amount or extent of spread, if we may use such an expression, toward the region which it supplies must be increased. It is not altogether surprising, therefore, that the levocardiogram is altered in the manner described. The chief difficulty arises in explaining why, during the last part of the *QRS*-interval when right ventricular effects should predominate, the electrical axis still maintains a right to left direction. It is hardly probable that the activation of that part of the left ventricular wall normally supplied by the anterior subdivision can be so greatly delayed as to permit it to play a prominent rôle in determining the position of the electrical axis at so late a period. It is possible, however, that because the dorsal part of the septum precedes the ventral part the excitation wave first reaches the right Purkinje system at a point much further to the right and much closer to the posterior wall than would otherwise be the case, and that the late right to left effects referred to are due to late activation of the conus. In the absence of more precise information than is now available it would be useless to speculate further.

It would seem that the effects produced by section of the posterior

subdivision of the left branch should be in a general way the reverse of those produced by cutting the anterior and this appears to be the case.

Before leaving this subject we should like to point out that it cannot be expected that section of the anterior subdivision will make the levocardiogram frankly discordant in all animals. It seems probable that it does so only in those dogs in which some tendency toward discordance is already present; possibly because of peculiarities of the conducting tracts of such a kind that the muscle supplied by the posterior subdivision of the left branch is activated earlier than in the average animal.

THE ORIGIN OF Q′

We must now turn to the earliest ventricular deflection of branch block curves; we refer to *Q′*. This wave is, on the whole, a more prominent feature of human than of canine curves. In the former it is almost always present; in the curves which we attribute to left branch block it is most prominent in Lead I and is absent in Lead III; in curves of the opposite type just the reverse is the case. In the dog's dextrocardiogram *Q′* is comparatively rare; when it occurs it is usually most prominent in Lead I, and absent in Lead III. In the levocardiogram it is common in Lead I; it is usually most prominent in this lead or in Lead II.

At first thought it seems obvious that *Q′* must be attributed to the excitation of the subendocardial muscle which is first to become active. To determine what region is first activated is, however, a matter of some difficulty. The excitation process spreads over the endocardial surface of the heart with great rapidity and even at the time when ventricular activity is just beginning many different points are passing into the active state at the same moment. Before the inscription of *Q′* is complete the excitation process has spread over a very large area.

Furthermore, endocardial readings are difficult to obtain and not entirely trustworthy. But even if the earliest point were known we could not be certain that *Q′* was written by effects which arose in the region in which this point lay. It is obvious that before an appreciable difference of potential can be recorded by indirect leads, a considerable mass of muscle must be involved. The rate at which the surface which separates active and resting muscle increases in a given region must depend upon the density of the Purkinje network, or rather the number of junctions per unit area between Purkinje and ordinary muscle fibers. It is quite possible that *Q′* is written not by the first region activated but by some region which is relatively early and which at the same time is activated with great rapidity. At the present time, therefore, any opinion as to the location of the muscle responsible for *Q′* must be based almost entirely upon the position of the electrical axis during its inscription.

If our conception of human branch-block curves is correct, Q' is probably not, if we may depend upon the criterion mentioned, of septal origin in man as Lewis apparently thought. It is difficult also to see how Q' of the canine dextrocardiogram can be due to septal effects; but Q' of the levocardiogram, on the other hand, may well be due to the activation of some region on the septal wall of the left ventricle. We have already referred to the curves published by Wilson and Herrmann[6] to show the effect of cutting the anterior subdivision of the left branch upon the levocardiogram. It is interesting to note that these curves show a distinct Q' in Lead I after this subdivision was cut although none was present before. It is possible that further information regarding this deflection may be obtained from the form of the curves recorded by means of direct leads in animals and by means of precordial leads in man.

VENTRICULAR PREPONDERANCE

In connection with his analysis of the human dextrocardiogram and levocardiogram Lewis[2] also made a detailed study of the clinical curves which are attributed to preponderant hypertrophy of the left and of the right ventricle respectively. In left preponderance he found a counter-clockwise, in right preponderance a clockwise rotation of the electrical axis. He expressed the view that hypertrophy of a single ventricle increases the magnitude of its electrical effects and thus enables them to dominate the bicardiogram. This hypothesis offered a logical and convincing explanation of the resemblance between the curves attributed to enlargement of one ventricle and those attributed to branch block on the opposite side.

It must be remembered, however, that when the right or left ventricle is hypertrophied, the increase in muscle mass is not confined to the lateral wall of the chamber affected, but involves the septal wall as well. If the excitation process reaches the two ventricles at the same time, approximately one-half of the septal muscle, must be activated from each side.

Let us suppose that the left ventricle is greatly hypertrophied; the mass of the septum must then be greatly increased. Consequently, the electrical effects produced by the activation of the septal wall of the right ventricle, that is to say, by the right half of the septum, will be greatly augmented, without a corresponding alteration in the electrical effects, produced by the free wall, to which they are opposed. If the dextrocardiogram is, as we believe, normally dominated by septal effects, it will be exaggerated either in amplitude, in duration or in both.*

*The idea seems to be prevalent in the literature that if there was any relation between the mass of the heart muscle and the amplitude of the electrocardiogram, a small animal should display curves of lesser amplitude than a larger one. This idea is based upon a misconception; it fails to take into consideration the quantity of the conducting material in which the heart is immersed, and the mean distance of the electrodes from the heart. An infant's heart in a man's body would produce a very small curve.

The electrical effects produced by the septal wall of the left ventricle will also be magnified, but since the forces opposed to them must undergo an even greater amplification, the levocardiogram may actually be smaller than that of a left ventricle of normal size. According to this point of view hypertrophy of one ventricle enables the opposite chamber to dominate the ventricular complex.

It is possible, however, to look at the matter from another standpoint. If the septum is activated from the right and left sides in equal measure, the sum of the electrical effects produced by the septal muscle must be very small. Consequently, we may say that in left ventricular preponderance the ventricular complex is dominated by effects produced by the hypertrophied lateral wall of the left ventricle. This statement is not equivalent to the assertion that it is dominated by the levocardiogram, if we are correct in believing that the chief deflections of the latter are of septal origin.

We come, therefore, to the conclusion that left ventricular hypertrophy and left branch block have a similar effect upon the electrocardiogram, because both increase the number of muscle units or the total quantity of muscle that is activated from right to left. In one case the point of stimulation, so to speak, is shifted to the right; in the other the center of mass is shifted to the left.

This explanation of preponderance curves is incomplete in one respect. It does not account for the fact that Q' is most prominent in Lead I, in left preponderance, and most prominent in Lead III in right preponderance. It is difficult to understand how the relative mass of the two ventricles can determine the order in which the subendocardial muscle, which must be responsible for the deflection, is activated. For this reason, Barker, Macleod and Alexander[1] suggested that there must be a defect in conduction in the special tissues of the enlarged ventricle. It is very probable that many of the clinical curves which are attributed to preponderant hypertrophy of one or the other ventricle are partly, if not entirely, due to this cause.

As an explanation of all preponderance curves this hypothesis meets, however, with the objection that in the newborn right ventricular preponderance is a normal phenomenon and cannot therefore be due to a conduction defect in the right branch of the His-bundle, although it might conceivably be due to a greater length of the conducting tracts in the large right ventricle. In the infant's curve Q is most prominent in Lead III and is absent in Lead I, just as it is in the right ventricular preponderance of mitral stenosis and congenital pulmonary stenosis.

In the normal human electrocardiogram Q is almost never present in all three leads; it is either most prominent in Lead I or in Lead III. In the first case Q must be attributed to the activation of some region of subendocardial muscle in the left ventricle; in the second, to a similar mass of muscle in the right ventricle. The muscle concerned is probably

on the free wall near the apex in each instance. The order in which, or the relative speed with which, these two regions are activated determines whether *Q* shall occur in Lead I or in Lead III. In some manner, as yet obscure, the enlargement of one ventricle enables the other to write this deflection.

THE INITIAL DEFLECTIONS OF THE NORMAL VENTRICULAR COMPLEX

The initial deflections of the normal ventricular complex may be regarded as the algebraic sum of the corresponding deflections of the dextrocardiogram and levocardiogram. Each normal deflection may consequently be considered a right ventricular effect if it is contributed by the former, a left ventricular effect if it is contributed by the latter.

This method of analyzing the normal ventricular complex is entirely justifiable, but in some respects it is confusing. We discover, for instance, that although *R* of Lead I and *R* of Lead III record the same phenomenon, the former is written by one ventricle, the latter by the other. Let us consider *R* of Lead I in greater detail. Both ventricles are producing effects at the time when it is being written. The septal wall of the right ventricle is producing effects which point in the positive direction; we will call the sum of these effects $(+ A)$. We may then represent the effects of the lateral wall of the right ventricle by $(- B)$, the effects of the septal wall of the left ventricle by $(- C)$, and the effects of the lateral wall of the left ventricle by $(+ D)$. The right ventricular effects will then be represented by $(A - B)$, the left ventricular effects by $(D - C)$, the total effect by $(A - B - C + D)$.

Let us suppose that the septal effects of the two ventricles are equal in magnitude although opposite in direction. The total effect will then be represented by $(D - B)$. *R* is positive because *D* is greater in magnitude than *B*. Since *D* represents the effects of the lateral wall of the left ventricle, *R* may therefore be considered a left ventricular effect. But since the sum of the right ventricular effects $(A - B)$ is positive and the sum of the left ventricular effects $(D - C)$ is negative, *R* is contributed by the dextrocardiogram. It is therefore a right ventricular effect. Whether *R* of Lead I is considered a right or a left ventricular effect is therefore merely a matter of the point of view.

If the septal effects included in the dextrocardiogram and the septal effects included in the levocardiogram are equal in magnitude but unlike in sign, they must cancel when these two curves are added. Consequently, no material error is made by neglecting the septal effects, so long as the two sides of the septum are excited simultaneously. The interpretation of the initial deflections of the electrocardiogram advanced by Lewis neglects the normal components produced by the activation of the septal muscle almost entirely. This is not unjustifiable when the right and left bundle branches are conducting normally, and his interpretation of the initial deflections written by the normal and by the

hypertrophied heart are not in conflict with the views presented here, except in so far as the significance of Q is concerned. When, however, there is a defect in condition in either bundle branch, the effects produced by the septum cannot, according to our view, be neglected. In disregarding them under these circumstances we believe that Lewis was in error.

For the reasons indicated above, we regard the following interpretation of the normal initial deflections as equally accurate and more simple, than that which attempts to separate the effects produced by the two ventricles. R of the bicardiogram may be attributed to the fact that during the early phases of the period of excitation all of the electrical effects except those produced by the apical muscle which lies opposite the valvular orifices in the cardiac base are opposed by forces equal in magnitude and opposite in sign. S may be attributed to unopposed forces produced by the basal muscle of both ventricles after the apical portions of the cardiac wall have been completely activated. It is possible that some muscle in the upper septum and in the conus arteriosus which seems to be poorly supplied with Purkinje tissue may contribute to this deflection. The origin of Q has already been discussed.

COMMENTS

We have attempted to give a complete explanation of the initial deflections of the ventricular complex of the electrocardiogram, consistent with the observations upon the exposed human heart recently reported by Barker, Macleod, and Alexander.[1] This explanation is based upon the observations made some years ago by Lewis and Rothschild[8] and by Lewis.[2] We have taken it for granted that these observations are correct in every particular. We have accepted without reservation the hypothesis advanced by Lewis that the electrical axis is determined by the average direction in which the excitation process is spreading. We believe, however, that some of the conclusions which Lewis drew from these observations are not well founded. We believe that he was misled by the histological studies of human branch block reported by Eppinger and Stoerk,[11] and by some observations upon the dog in which in attempting to place a clamp upon the right branch he injured conducting tracts on the left side of the septum.

We believe that the interpretation of the initial deflections of the electrocardiogram given in this article is sound in theory and correct so far as its major features are concerned. As regards minor details it must be considered tentative only. Many of the problems which we have attempted to solve are decidedly complicated and much desirable information bearing upon them is not available. In discussing problems of this kind from the theoretical standpoint it is necessary to make many simplifying assumptions; the magnitude of the errors thus introduced is difficult to estimate accurately. Furthermore, it is not

possible to be certain that all of the factors involved in the problems attacked have been correctly evaluated and that none have been overlooked.

CONCLUSIONS

The view advanced by Barker, Macleod, and Alexander, that the clinical electrocardiograms heretofore ascribed to right branch block are due to left branch block and *vice versa*, is not necessarily in conflict with the hypothesis that the electrical axis at a given instant points in the average direction in which the excitation process is spreading at that moment.

Both the dextrocardiogram and the levocardiogram, canine and human, are dominated by electrical effects produced by the ventricular septum.

Preponderant hypertrophy of one ventricle increases the magnitude of the electrical effects produced by the opposite ventricle by increasing the mass of its septal wall without altering its lateral wall.

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PARAFFIN INFILTRATION OF HEARTS

A Permanent Method for Preservation*

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INFILTRATION of organs with paraffin is a relatively old procedure, the general principle being to dehydrate the fixed organ and to infiltrate it with paraffin much as is done in the routine manner for blocking tissues. An organ thus treated has the following properties: (1) it is very easy to handle and is therefore excellent for teaching purposes; (2) the normal topographic relations of the organ are retained; (3) the tissues are permanently fit for histological studies.

Our purpose in writing this report is to describe in some detail a method of paraffinizing hearts which is simple and permits the retention of the original topographic relations in excellent condition. While the technic described is based on its application to the heart, it can be used with slight modification for other organs.

METHOD

The unopened heart is obtained as soon after death as possible and a description given. In order to examine the interior of the heart so that a macroscopic diagnosis may be immediately available, it has been our practice to use an electrically lighted nasal speculum, such as the Cameron Diagnostoscope with adjustable trigger Nasoscope Head. During this examination the larger masses of blood clot should be removed. Special glass cannulas are now tied into the aorta, pulmonary artery, superior vena cava and one of the pulmonary veins. The cannulas should be almost of the same size as the orifices into which they are tied and they should have a small sloping flange (Fig. 1). In order to block the other pulmonary vein orifices, the inferior vena cava and any other holes which may have been made in the auricles during the autopsy, wooden pulleys of various sizes‡ are used (Fig. 2). As in the case of the cannulas, the size of the pulleys should be as nearly as possible the size of the hole to be blocked up.

The pulley is placed into the hole and the auricular tissues are tied around the groove by means of a thread. The purpose of this procedure is to prevent the puckered appearance and collapse of the auricles

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†Aided by a grant from the Lucius N. Littauer Research Fund.
‡We find it convenient to use pulleys 1 cm. in width and 1, 2, 3, 4, 5 and 6 cm. respectively in diameter.

which results from merely tying the tissues together around the hole.

Short lengths of rubber tubing are attached to the pulmonary artery and aortic cannulas and are joined together by means of a glass "Y" tube. A hook is passed under the "Y" tube and the heart is in this way suspended from a stand (Fig. 3). Short lengths of rubber tubing are also attached to the cannulas inserted into the auricles, and these are individually suspended from the stand in such a manner that all pressure is taken off the auricles and no distortion of the auricular walls is produced. In other words, the cannulas should be so suspended that their main axis is parallel to the pulmonary vein and superior vena cava respectively.

The suspended organ is lowered into a container of approximately three liters capacity. The apex of the heart should reach to about 3 cm. above the bottom of the container. A large tank containing neu-

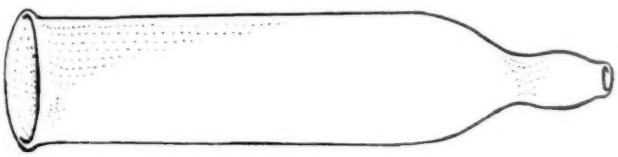

Fig. 1.—Type of glass cannula tied into aorta, pulmonary artery, superior vena cava and one of the pulmonary veins.

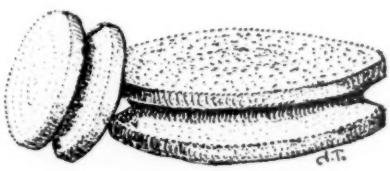

Fig. 2.—Type of wooden pulley used for blocking orifices in heart.

tralized formaldehyde sodium chloride solution* is placed on a shelf approximately 2 feet above the level of the apex of the heart. This is now attached to the "Y" tube and the formalin allowed to fill the chambers of the heart in this retrograde manner.

In most of the specimens the semilunar valves are sufficiently incompetent to allow the formalin to flow backward through the ventricular and auricular systems. In this way air is driven up the auricular cannulas, and as soon as the formalin appears the rubber tubes connected to these cannulas are clamped off. In those instances where the semilunar valves are competent it is necessary first to fill the auricular and ventricular systems through the auricular cannulas. When this is accomplished the auricular cannulas are tied off and perfusion is continued through the arterial cannulas. The shrinkage of the valves which takes place in the formalin generally eventually

*Solution of formaldehyde, U. S. P., 10 parts; 1 per cent sodium chloride solution, 90 parts. This solution is rendered neutral with a weak alkali.

accomplishes the desired result of allowing the fixing fluid to pass by the semilunar valves.

The heart having been set up and filled in the manner indicated, the container in which the heart hangs is now filled with formalin until it reaches above the level of all exposed tissue. Twenty-four hours later the formalin inside and outside the heart is replaced by fresh formalin. This is repeated for a third time twenty-four hours later.

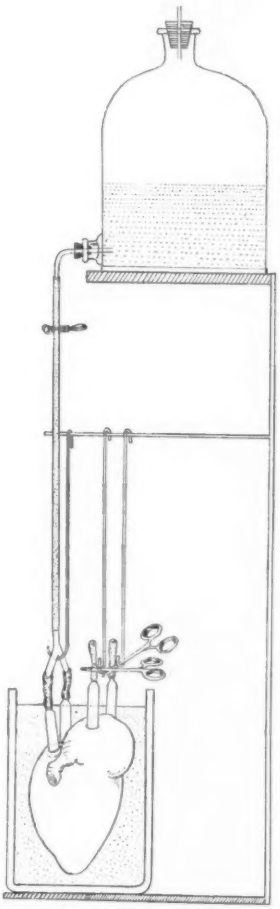

Fig. 3.—Method of suspending heart and perfusing with formalin.

If it is so desired, blocks of tissue may now be cut from the heart, although it is advisable to delay this as long as possible.

After complete fixation in this manner the cannulas are carefully removed, the wooden pulleys, however, being left in place. The heart is now gently dried with a towel and placed into a container holding approximately 2-2½ liters of 65 per cent alcohol. The heart should be placed on a bed of cotton and, depending on its size, should remain

in the container for approximately twenty-four to forty-eight hours. The organ is passed through increasing percentages of alcohol (80 per cent, 90 per cent, 95 per cent and absolute), again leaving it in each of these fluids for twenty-four to forty-eight hours. It is advisable to sponge the heart gently with a dry towel between these stages.

After the last procedure, measure the strength of the alcohol by means of an alcoholometer. If this measures less than 98 per cent, place into fresh absolute alcohol. After forty-eight hours test again. Continue these changes until the absolute alcohol remains at least 98

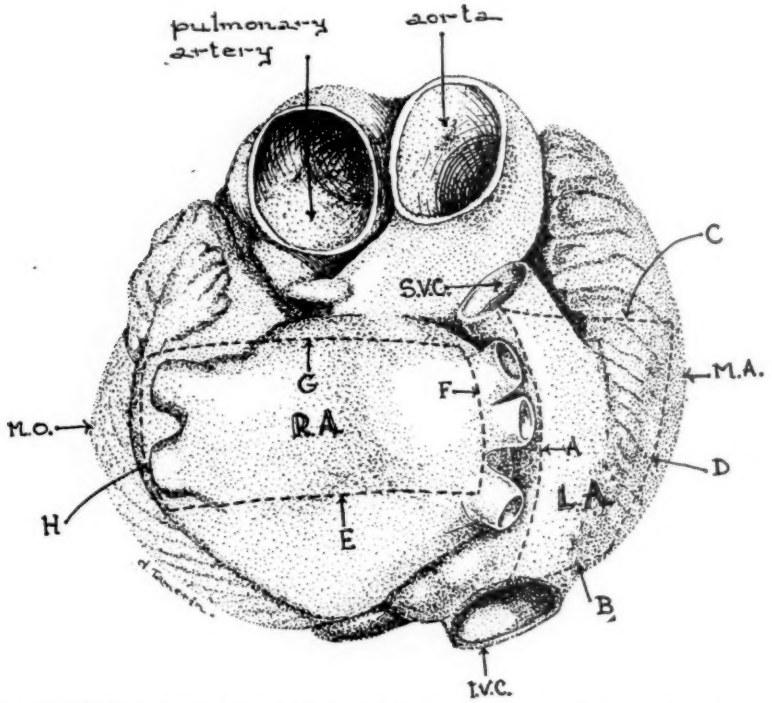

Fig. 4.—Method of opening auricles. *I.V.C.* = inferior vena cava. *S.V.C.* = superior vena cava. *L.A.* = left auricle. *R.A.* = right auricle. *M.A.* = margo acutus. *M.O.* = margo obtusus.

per cent. The last stage of dehydration from about 96 per cent alcohol can be expedited by placing the organ in fresh anhydrous acetone. We prefer absolute alcohol.

Place into toluol for forty-eight hours. Change into fresh toluol for twenty-four hours. Drain off the toluol rapidly and place into the following mixture kept in a paraffin oven at 56 degrees:

Paraffin, melting point 53-55 C.	95 parts by weight
Pure unbleached beeswax	5 parts by weight

Keep in an incubator for twenty-four hours. Transfer to another paraffin-wax bath for twenty-four hours. Remove from bath, insert

a hook into the apex and suspend the organ upside down in order to allow the excess paraffin-wax to drain off.

While the heart is still slightly warm it should be opened in the following manner:

Insert a knife into the inferior vena cava, the edge pointing toward the anterior surface of the heart. Push the blade through the superior wall of the right auricle until the superior vena cava is reached, cutting as close to the interventricular septum as possible (Fig. 4 *A*). Reinsert the knife into the inferior vena cava with the edge pointing

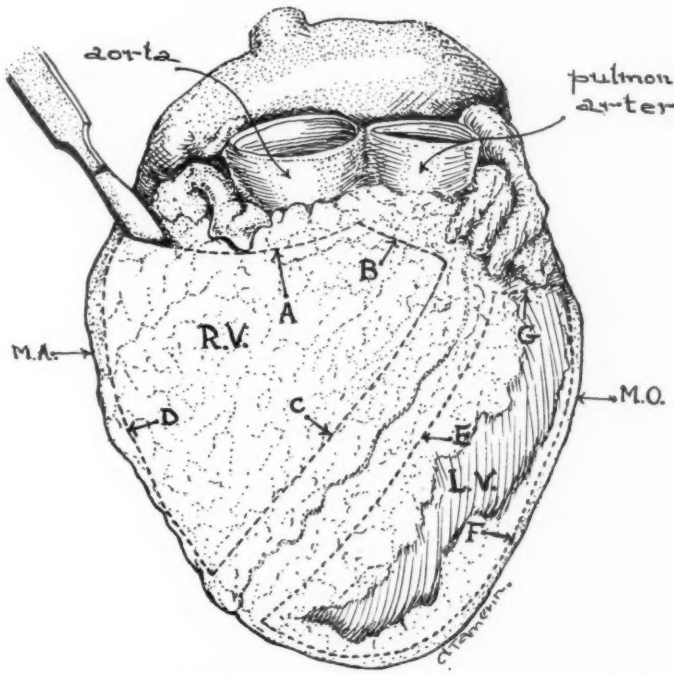

Fig. 5.—Method of opening ventricles. *M.A.* = margo acutus. *M.O.* = margo obtusus. *L.V.* = left ventricle. *R.V.* = right ventricle.

toward the margo acutus. Make an incision over the superior wall of the right auricle parallel to its posterior wall until the auriculo-ventricular sulcus is reached (Fig. 4 *B*).

Insert the knife into the superior vena cava with the edge pointing toward the margo acutus. Make an incision along an imaginary line which joins the superior vena cava with a point 5 mm. posterior to the junction of the inferior border of the right auricular appendix with the auriculo-ventricular sulcus (Fig. 4 *C*). Connect the distal point of this incision with the posterior auricular incision previously made (Fig. 4 *D*). In this manner the top of the right auricle is easily removed.

Trim the pulmonary artery to within a centimeter of the level of the valve commissures, and the aorta to any level desired. Insert the point of the knife slightly below the right auriculo-ventricular sulcus at the junction of the latter with the margo acutus. The edge of the knife should point toward the pulmonary artery, the blade being held in such a manner that the knife forms an angle of approximately 45 degrees with the upper segment of the main axis of the heart and 135 degrees with the lower segment (Fig. 5). Push the blade through the myocardium into the right ventricle being careful not to strike the delicate tricuspid valve. Carry the blade forward following the contour of the auriculo-ventricular sulcus until the incision reaches to within ½ cm. of the lower border of the pulmonary cusps (Fig. 5 *A*). This can be seen by looking down the pulmonary orifice.

Turn the blade downward and continue this incision parallel with the plane of the pulmonary cusps until the interventricular septum is reached (Fig. 5 *B*). Now turn the blade edge down and carry the incision to the apex of the right ventricle, keeping the knife at all times close to the interventricular septum (Fig. 5 *C*). This incision can be easily watched through the pulmonary orifice.

Insert the blade of the knife into the margo acutus at the first point of the original ventricular incision, i.e., below the junction of the auriculo-ventricular sulcus and the margo acutus, and carry the incision down to join the last part of the interventricular cut (Fig. 5 *D*). While this incision is being made, look through the tricuspid orfice to make sure that the tricuspid valve is not injured. Gently raise this window of right ventricular myocardium. It will be found that the trabecula septomarginalis or the anterior papillary muscle makes it impossible to remove completely the myocardial segment. This connection is severed by the knife at a convenient site, and the right ventricular chamber is thus opened for inspection.

Insert the blade of the knife through one of the pulmonary veins (preferably the right posterior) with the edge pointing toward the margo obtusus (Fig. 4). Make an incision across the superior wall of the left auricle until the auriculo-ventricular sulcus is reached (Fig. 4 *E*). Starting with the first point of this incision turn the knife edge anteriorly and cut through the superior wall of the left auricle until a point is reached on the latter approximately opposite the superior vena cava of the right auricle (Fig. 4 *F*). Turn the edge of the knife toward the margo obtusus and make an incision along a line which runs to approximately 5 mm. posterior to the junction of the left auricular appendix with the auriculoventricular sulcus (Fig. 4 *G*). Complete the incision parallel to the line of the auriculo-ventricular sulcus (Fig. 4 *H*). This frees the left auricular window and thus an opening is made into the left auricle leaving enough of the posterior wall of the latter to show pathological lesions.

The last and most difficult incision remains. Insert the knife blade into the anterior wall of the left ventricle at a point approximately 1 cm. below the junction of the left coronary artery with the left anterior descending branch (Fig. 5). The cutting edge should point toward the inferior border of the interventricular septum. Watching the contour of the interventricular septum and estimating the thickness of the latter as closely as possible, make an incision parallel to the right interventricular incision (Fig. 5 *C*) with the object in mind of exposing as much left ventricle as possible without actually cutting into the interventricular septum (Fig. 5 *E*). The incision should be carried as far as the margo acutus.

Insert the knife at a point 1 cm. below the auriculo-ventricular sulcus at the latter's junction with the margo obtusus with the cutting edge pointing toward the apex of the heart. Look through the mitral valve orifice to make sure that the mitral cusp is not perforated by the point of the knife. With the blade penetrating through the entire thickness of the left ventricular wall carry the incision down to the apex of the heart and continue it around the apex until it joins the left interventricular incision described above (Fig. 5 *F*). Make a connecting incision between the upper ends of the interventricular and margo obtusus incision (Fig. 5 *G*).

If the tissue has been cleanly cut it will be found possible to raise slightly the lower border of this left ventricular flap. It will be impossible, however, to remove the flap because of the stout left anterior papillary muscle which binds it to the mitral flap. The papillary muscle is severed close to its apex by a knife, and the left ventricular flap is thus removed. Carefully clean out all blood clot.

If the opening of the heart is performed, as it should be, while the myocardium is slightly warm, it will be found very simple to remove whatever blocks are necessary for microscopic study. In order to examine the coronary arteries, however, it is desirable that coronal incisions of the vessels should be made during one of the dehydration stages in alcohol. Blocks can then be removed. If at some future occasion it is necessary to cut additional blocks from the heart, it should be placed in a 56 degree incubator for about fifteen or twenty minutes until the paraffin softens.

THE CARDIODYNAMIC EFFECTS OF ACUTE EXPERIMENTAL MITRAL STENOSIS*

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A DIFFERENCE of opinion exists in regard to the cardiodynamic effects of acute mitral stenosis, experimentally produced, except all are agreed that the left intra-auricular pressure is elevated. Invariably, acute mitral stenosis when produced in animals with intact circulation was found to elevate the pressure in the pulmonary artery (in severe stenosis, in the right ventricle also) and to lower the pressure in the left ventricle, systemic arteries and veins (Kornfeldt,[16] 1892; Gerhardt,[8, 9] 1901, 1912; MacCallum and McClure,[17] 1906; Hirschfelder,[10] 1908 and Dzwankowska,[7] 1924). On the other hand, similar experiments made on the heart-lung preparation by Straub,[19] 1917, showed only a transient fall in pressure in the left ventricle and systemic arteries, and a fall in the maximum pressure of the right ventricle accompanied by an unchanged initial pressure. The question arises whether the results of Straub indicate that the heart-lung preparation is unable to predict what happens in the animal when its circulation is intact, or, on the other hand, whether the graphic method used by the other investigators failed to depict the true state of affairs.

Mitral stenosis is perhaps the valvular defect most difficult to produce experimentally. Preliminary experiments soon convinced us that some of the discrepancy in previous results was caused by artefacts inherent in certain methods of producing mitral stenosis. In these preliminary trials several of the methods previously described were tested, e.g.: the suture method (MacCallum and McClure,[17] 1906, Hirschfelder,[10] 1908 and Allen,[1] 1924); invagination of the left auricle through the A-V ring; compression of the mitral ring manually or, as suggested by MacCallum,[17] 1906, Cushing and Branch[5] 1907, and Hirschfelder,[10] 1908, by clamp or suture.† The artefacts were produced in three chief ways: (1) by clotting of blood, (2) by traction and (3) by compression of the coronary arteries.

Since the results of mitral stenosis can be influenced by these artefacts, a few words on the effects of these artefacts and on the ways in which they were avoided or discounted is given. Traction in producing the mitral stenosis may lead to an aortic stenosis also. This was found

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†Scarifying the valves by strong alkali, radium of microorganisms as suggested by Coryllos, Edwards and Bagg,[4] 1923, and by Cutler, Levine and Beck,[6] 1924, was not tried as it was not suited for our purposes. We felt that we could not produce a stenosis of sufficient degree with Straub's valve method.

to be the case when mitral stenosis was produced after an animal's death. In the living animal changes in the intraventricular and aortic pressure curves, which resemble those described in aortic stenosis by Katz, Ralli and Cheer[13] (1928), and which are quite different from the effects of mitral stenosis, could be produced by traction at the mitral ring (cf. Fig. 1). Traction also tends to displace the position of the manometer cannulae, especially in the left auricle, where the pressure level could be varied at will by application of suitable traction.

A diminution in the volume of the left auricle and left ventricle occurs with most methods of producing a mitral stenosis. At the same time there is a tendency to force blood into the left ventricular cavity. These changes also will lead to artefacts.

When mitral stenosis is produced by compression of the A-V ring there is a tendency to occlude the left circumflex coronary artery,

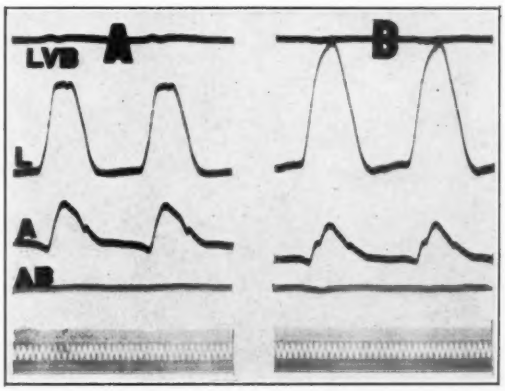

Fig. 1.—Pressure curves from aorta, *A*, and left ventricle, *L*, showing result of improper production of mitral stenosis which leads to concomitant aortic stenosis. Segment *A* is control; *B*, after mitral and aortic occlusion. *LVB* and *AB* base lines for left ventricular and aortic pressure curves respectively. Time below, each double vibrations, 1/50 sec. Note that in segment *B* the level and amplitude of the left ventricular pressure curve rose while they fell in the aortic curve; note also the anacrotic interruption which develops in the latter curve.

leading at once to serious undesirable disorders of the heart. Bernheim[3] (1909), Schlepelmann[18] (1912) and Cutler, Levine and Beck[6] (1924) have modified the suture method to avoid this difficulty.

METHODS

In the present research a ligature method was employed to produce the mitral stenosis which with due care minimized the foregoing artefacts. The circumflex coronary artery was avoided by placing two ligatures on the auricular side of the A-V groove, but close to it. One of the ligatures was fastened to the anterior wall of the left auricle near its junction with the aorta, the other to the posterior wall of the left auricle near the interauricular groove. The two ligatures were kept in place by threading them through a series of loops fastened to the wall of the left auricle close to the A-V groove. Traction on these ligatures caused a constriction, the extent of which could be varied up to "button-hole" proportions without inter-

fering with the coronary supply of the ventricles* and without producing a concomitant aortic stenosis. The absence of aortic stenosis was shown by the parallel changes in the pressures of the aorta and left ventricle unlike the changes seen in Fig. 1, and by repeating the traction post mortem. The patency of the

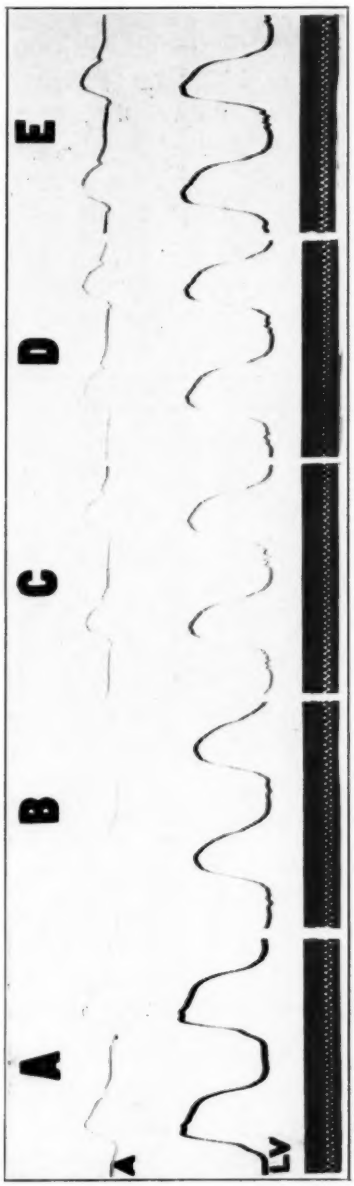

Fig. 2.—Pressure curves from aorta, *A*, and left ventricle, *LV*, showing immediate and later effects of mitral stenosis. Segment *A* is control, *B*, immediately and *C*, *D*, and *E* various periods within ten minutes after mitral stenosis produced. Time as in Fig. 1. Note appearance of presystolic oscillations in segments *B*, et seq.

coronary vessels was similarly tested post mortem. Care was taken to make the stenosis slowly and steadily with a minimal displacement of the heart. In this way traction effects were avoided or at least minimized. It was not possible to

*An unavoidable interference occurred with the blood supply to the left auricle which was not serious, we believe, because of the abundant Thebesian supply.

avoid the deformation and alteration in size of the left auricle and ventricle, but the effects of this complication are easily evaluated and do not interfere with the analysis of the effects of the mitral stenosis.

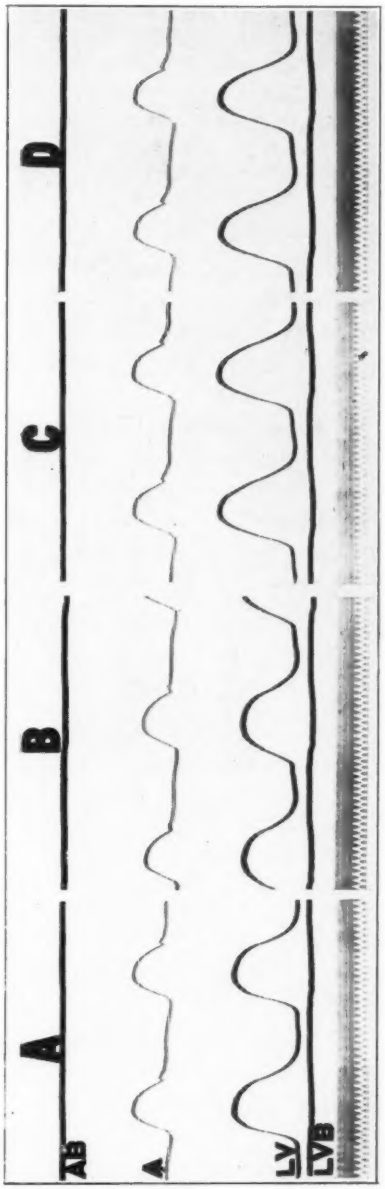

Fig. 3.—Pressure curves from aorta, *A*, and left ventricle, *LV*, showing immediate and later effects of mitral stenosis. Segment *A* is control, *B* immediately and *C* and *D* later periods after mitral stenosis. *AB* and *LVB* and time as in Fig 1.

The changes in the pressure pulses following mitral stenosis were studied by registering the curves on bromide paper with manometers of the Wiggers' pattern[20] (1928). The experiments were made on twenty-two anesthetized dogs with chest open and artificial respiration. Simultaneous pressure records were obtained without parallax with the duo-slit lamp of Katz and Baker[12] (1924) in the following

combinations: left ventricle and aorta; left ventricle and left auricle; aorta and left auricle; left auricle and pulmonary artery; pulmonary artery and right ventricle; pulmonary artery and aorta. The manometers were inserted in the usual manner (cf. Wiggers,[21] 1928) except for the following slight modifications: the manometer for the left auricle was inserted via a branch of the left lower pulmonary vein; the manometer for the pulmonary artery was inserted directly through the wall (cf. Katz and Weinman,[15] 1927), or via the left pulmonary artery so that the opening was within 1 cm. of the semilunar valves. The sensitivity of the manometers was determined but the curves were not calibrated as we were interested only in relative changes. In several experiments direct readings of the right and left auricular pressures were made with saline manometers.

RESULTS

(a) *Effect on heart rate and the duration of the systolic phases.*—The changes in heart rate were analyzed in detail in 63 experiments made on 15 dogs. In most of these experiments no essential change in rate occurred (e.g., Figs. 4, 6 and 7). In 20 experiments the rate

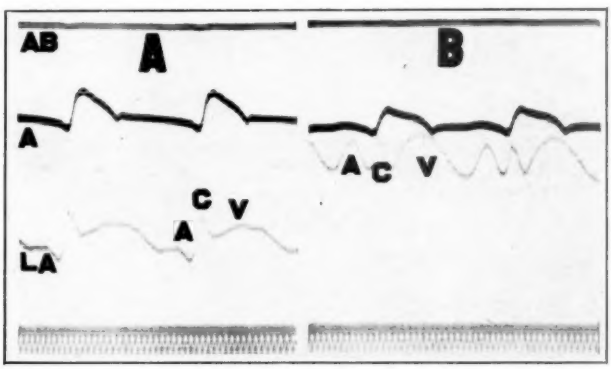

Fig. 4.—Pressure curves from aorta and left auricle showing effect of mitral stenosis. Segment *A* is control; segment *B*, immediately after mitral stenosis. *AB* aortic base line, *A*, aortic pressure curve; *LA*, left auricular pressure curve with so-called *A*, *C* and *V* waves labelled. Time as in Fig. 1.

was slowed (e.g. Figs. 3, 8), in some markedly. A slight increase in rate occurred in seven experiments (e.g. Fig. 2). Sectioning the vagi did not alter the rate response, indicating that the vagi had little to do with the rate changes. Manipulation of the auricles or traction on ligatures without producing a stenosis caused no changes in heart rate. It would seem that the rate changes, when they occurred, were caused by an alteration in the blood supply to the sinus node.

An abbreviation of total systole of the left ventricle was noted in 20 out of the 29 experiments analyzed (e.g. Figs. 2, 3)—in some instances this occurred despite a lengthening of the cycle (e.g. Fig. 3). In six experiments systole remained unchanged presumably because the tendency of the slowing in heart rate to prolong systole balanced the tendency for the stenosis to abbreviate systole. In the three experiments where the slowing of the rate was most marked systole was prolonged.

The changes in the ejection phase of the left ventricle were similar to those in total systole, i.e., an abbreviation in 29 out of 36 experiments in which it was measured (e.g. Figs. 2, 3, 4 and 8), no change in four, and a prolongation in three. The changes in the isometric contraction phase were less striking; a slight abbreviation was found in 16 out of 29 experiments measured, no change in 10, and a slight prolongation in three.

The striking abbreviation of systole and ejection of the left ventricle could be explained either (1) by the decrease in initial distention of the heart which has been shown to produce this change (Wiggers and Katz,[22] 1922) or (2) by the direct action of the diminished coronary flow following mitral stenosis which accompanies the fall in aortic pressure. Our observations showed a similar decrease in systole and ejection in the right ventricle in every experiment where these phases were measured, i.e., four experiments in which systole was measured

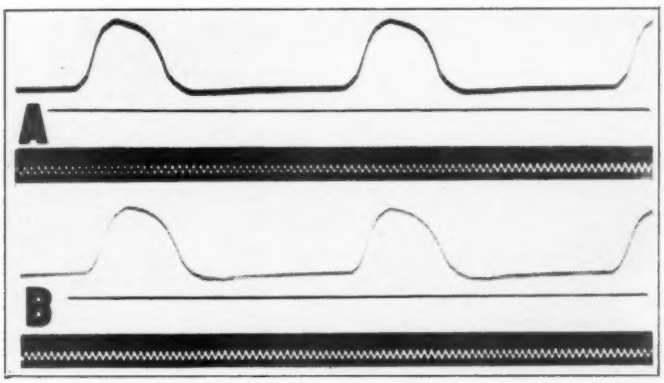

Fig. 5.—Pressure curves from left ventricle during vagus slowing showing effect of mitral stenosis. Segment *A* is control; *B*, immediately after mitral stenosis. Time as in Fig. 1. Horizontal lines were inked in to permit comparisons of the gradient of curves during diastole.

and 15 experiments in which ejection was measured (e.g. Figs. 6, 7 and 8). The fact that this abbreviation occurred in spite of an increased distention of the right ventricle in several instances (e.g. Fig. 6) would indicate that the abbreviation of systole and ejection in both ventricles were caused to a large extent by the diminution in coronary flow which follows the fall in arterial pressure.

(b) *Effects on left auricular, left ventricular and aortic pressure curves.*—1. Immediate effects. On *a priori* grounds, a high-grade obstruction at the mitral orifice should diminish the filling of the left ventricle and as a consequence the initial pressure and the maximum pressure developed by the left ventricle during contraction should decrease. The aortic pressure level and pulse pressure should be lowered for the same reason.

A decrease in the pressure developed during contraction by the left

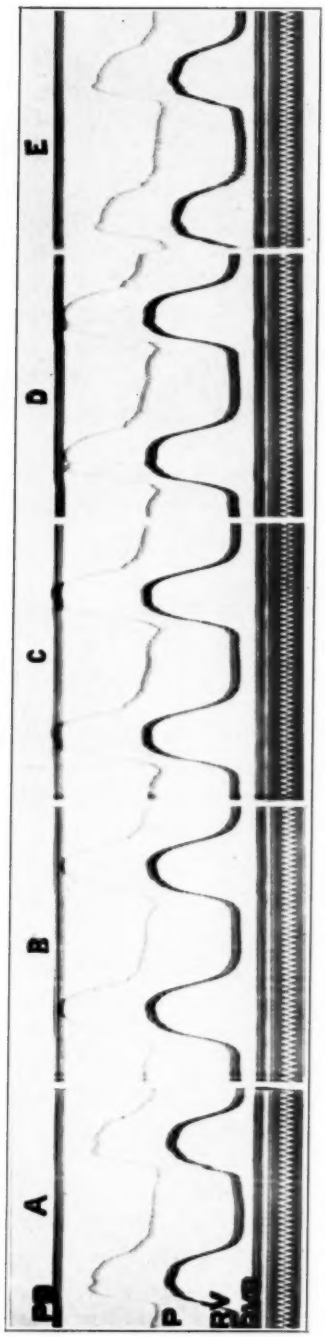

Fig. 6.—Pressure curves from pulmonary artery, *P*, and right ventricle, *RV*, showing immediate and later effects of mitral stenosis. Segment *A* and *E* are controls; *B*, immediately after mitral stenosis, *C*, *D*, later during mitral stenosis. *PB* and *RVB* are base lines for pulmonary arterial and right ventricular pressure curves. Time as in Fig. 1.

ventricle was found consistently just after obstructing the mitral orifice. This change was sometimes accompanied by a fall in initial pressure (cf. Fig. 2 *A* and *B*), but in most instances the initial pressure either remained unchanged or increased slightly (cf. Fig. 3 *A* and *B*). This unexpected change in initial tension is caused by an unavoidable artefact. The method of producing the stenosis leads to a deformation of the ventricular cavity which tends to increase the ventricular pressure temporarily by tending to decrease the ventricular volume, and this artefact counterbalances the tendency for the initial pressure to drop as a result of a decrease in filling. It is also possible that the change in position of the heart in relation to the manometer cannula may be the cause of the artefact.

In several experiments presystolic oscillations were recorded on the left ventricular pressure curve (cf. Fig. 2). The aortic pressure level and also the amplitude of the pulse decreased following stenosis in practically all cases (e.g. segment *B*, Figs. 2, 3, 4 and 8). This fall in

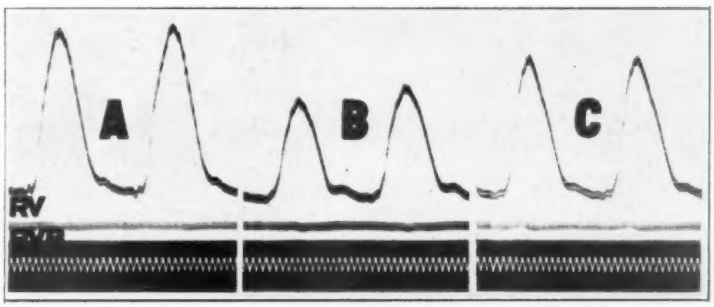

Fig. 7.—Pressure curves from right ventricle, *RV*, showing immediate and later effects of mitral stenosis. Segment *A* is control, *B* immediately after mitral stenosis, *C*, later during mitral stenosis. *RVB*, base line for pressure curve. Time as in Fig. 1.

aortic pressure level would tend to cause a decrease in the coronary flow. In several experiments, however, there was an elevation of the diastolic pressure although the systolic and pulse pressures decreased and the heart rate remained unchanged. This rise in diastolic pressure was apparently caused by a reflex vasoconstriction, since sectioning the vagi abolished it entirely.

2. Compensatory Effects.—The decrease in pressure development of the left ventricle and the lowering of the pulse pressure and pressure level of the aorta were not permanent, but after a variable time these pressures tended to increase again toward (e.g. Figs. 2, 3 and 8), and occasionally beyond, normal values (e.g. Fig. 3). Four mechanisms by which this change was brought about suggest themselves. In the first place, the elevation in the left auricular pressure which we found in every instance when traction effects were eliminated (e.g. Fig. 4) tends to overcome the handicap of the increased resistance to flow offered by the mitral stenosis. In the second place, the pumping action of the

left auricle is augmented as a result of the auricular distention. This augmentation in auricular activity goes hand in hand with the auricular distention. It is demonstrated by the increase in the *A* wave of the left auricular and left ventricular pressure curve (cf. Figs. 2 and 4). In the third place, there is a consistent prolongation of the time for filling which accompanies the abbreviation of systole. The ventricle therefore has not only a greater filling pressure head but also a longer time to fill. In the fourth place, there is an augmentation in the aspiration action of the ventricle (cf. Katz,[11] 1930). With filling hindered the relaxing ventricle will cause a greater drop in pressure at the start of filling, thereby increasing the pressure difference between the auricle and ventricle and so tending to facilitate the flow of blood. That this mechanism is operating is suggested by the fact that the difference in level between the start and end of filling is increased in every instance after mitral stenosis (compare segment *A* with segment *B C D* of

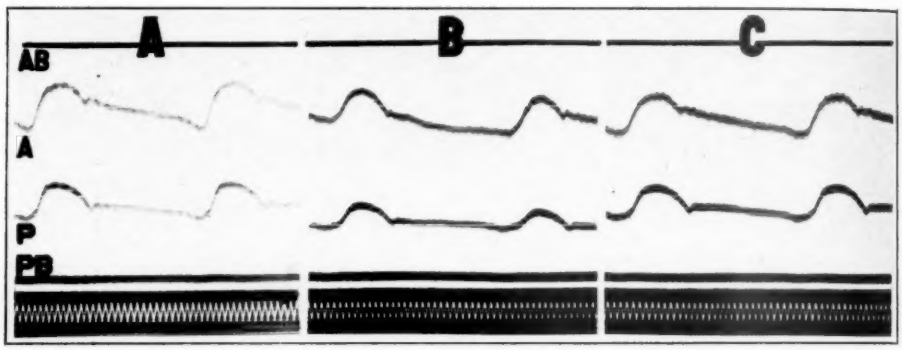

Fig. 8.—Pressure curves from aorta, *A*, and pulmonary artery, *P*, showing immediate and later effects of mitral stenosis. Segment *A* is control; *B* immediately after mitral stenosis; *C* later during mitral stenosis. *AB* and *PB* are base lines for aortic and pulmonary arterial pressure curves. Time as in Fig. 1.

Fig. 3). Part of this difference may be due to increase in auricular activity; however in certain experiments where a vagal slowing was produced and the auricular contribution minimized a similar increase in the difference in pressure level between the beginning and end of diastole was found (cf. segments *A* and *B* of Fig. 5). In Fig. 5 this increase in the pressure difference is caused by a greater drop at the start of filling and not by any rise at the end of filling as might be expected if an augmentation in auricular contribution were the cause.

(c) *Effect on right ventricular and pulmonary arterial pressure curves.*—Analysis of our experiments show two opposite effects on the right ventricular and pulmonary arterial pressure curves. In some experiments the initial pressure (and the pressure level in the right auricle) rises, and accompanying this there is an increase in the pressure development in the right ventricle (e.g. Fig. 6), and an increase in the systolic, diastolic and pulse pressures of the pulmonary artery

(e.g. Fig. 6). This is in agreement with the findings previously reported by us[13] (1929) in stenosis of the aorta. The cause is, of course, the "damming back" of blood in the pulmonary circuit and right ventricle. On the other hand, in other experiments the initial pressure and pressure development of the right ventricle decreased after mitral stenosis (e.g. Fig. 7) and with it the pressure level and pulse pressure of the pulmonary artery also decrease (e.g. Fig. 8). This change is attributed in part to the decrease in flow in the systemic vessels and coronaries leading to a diminution of the venous return to the right heart; in part this change must also be ascribed to the depression of both ventricles caused by the lowered coronary flow. The last factor is very important as it is the chief difference which exists between these mitral stenosis experiments and those of stenosis of the aorta previously reported. In a few experiments the adjustment between the effects of "damming back" on the one hand and those of reduced venous return and diminished coronary flow on the other was so nice that no changes in pressure were recorded. In many experiments the diastolic pressure in the pulmonary artery rose even though the systolic and pulse pressures fell. This combination was due to the effect of the "damming back" of blood in the pulmonary artery raising the pressure level, combined with the effect of a decreased venous return and coronary flow depressing the activity of the right ventricle of which the pulse pressure was an index. The fact that evidence of "damming back" of blood is present in some of these experiments indicates that in the intact animal such changes can occur even when the coronary flow is decreasing. This observation is contrary to Anrep's[2] (1925) results with the heart-lung, and shows that the heart-lung cannot be used to estimate the dynamic changes which occur in the intact circulation.

During compensation the curves gradually tended to return toward normal (e.g. Figs. 6, 7 and 8).

SUMMARY

1. A ligature method was developed to produce stenosis of the mitral orifice with a minimum of artefacts due to traction and with no interference with the coronary supply to the ventricle. The cardiodynamic changes were studied in dogs by optical manometers recording on bromide paper. The importance of recognizing, minimizing and evaluating the effects of artefacts is emphasized.

2. Experimental stenosis of the mitral orifice produced the following immediate changes:

a. A variable amount of slowing of the heart rate in most cases.
b. A marked abbreviation of the ejection and total systole time in both ventricles.
c. An elevation in the pressure of the left auricle.
d. An increase in the magnitude of the left auricular contraction.

e. A decrease in the maximum pressure developed by the left ventricle.

f. A variable change in the level of the initial pressure of the left ventricle (due to an unavoidable artefact).

g. A fall in systolic, diastolic and pulse pressure in the aorta.

h. A variable change in the pulmonary arterial and right ventricular pressures; the pressures sometimes fell, sometimes rose or remained unchanged.

i. The occasional appearance of presystolic oscillations on the left ventricular pressure curve.

j. A steeper gradient of pressure rise during diastasis in the left ventricular pressure curve.

3. These changes are in part the direct result of the stenosis, causing impediment of flow to the left ventricle and "damming back" of fluid in the pulmonary circuit. In part they depend on the decrease in coronary flow resulting from the fall in arterial blood pressure.

4. Compensatory mechanisms soon tend to restore conditions toward normal. Evidence is given which suggests that these compensatory mechanisms include: (a) an increase in the pressure head of the left auricle, (b) an increase in the magnitude of auricular activity, (c) a prolongation of the time for diastolic filling, and (d) an augmentation of the aspirating action of the left ventricle as evidenced by the steeper rise of the diastolic portion of its pressure curve. All these factors tend to overcome the impediment of the obstruction, thereby augmenting left ventricular filling and lessening the damming up of blood in the pulmonary circuit.

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EXPERIENCES WITH THE DERMATHERM (TYCOS) IN RELATION TO PERIPHERAL VASCULAR DISEASE

I. Normal Studies*

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THE study of the various pathological conditions of the extremities which are due to an inadequate blood supply has long been hampered by the lack of satisfactory methods of determining both the total blood supply to the part and the relative weight to be assigned in any given case to the factors of vascular occlusion and vascular spasm.

Numerous studies of the circulation of the extremities have been attempted, but none has given complete satisfaction. Slow cumbersome methods have had the additional disadvantage of gross inaccuracy. Palpation gives information for the lower extremity only in regard to gross changes in the major vessels in four situations, i.e., the femoral artery in the groin, the popliteal artery in the popliteal space, the posterior tibial at the ankle, and the dorsalis pedis. No clue is given as to the state of these vessels at other points or the possible development of anastomotic channels.

Stewart[1] studied the circulating blood volume in the extremities by elaborate calorimetric methods and succeeded in establishing a minimum value for circulating blood volume per unit weight in normal extremities. His method required an exacting technic and was not suitable for use outside the physiological laboratory. It also possessed the additional disadvantage of not giving differential results in the various regions of the extremities.

Cohen[2] and Stern[3] introduced the saline wheal test as a measure of the blood supply in arterial disturbances of the extremities and set up clinical standards for its use. This test measures the relative speed of imbibition of an intradermal saline wheal by the surrounding tissues and hence is only an indirect index to the local blood flow.

Starr[4] has recently brought forward the histamine test and used it rather extensively in arteriosclerosis and cases of diabetes mellitus with and without gangrene.

The Pachon oscillometer has proved a valuable adjunct to the study of vascular diseases but takes no account of the slow ooze of blood through minor vessels. In addition, the instrument is easily

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deranged and difficult to employ in clinical work as it requires the absolute cooperation of the patient.

D'Oelsnitz and Cornil[5] introduced the method of paralyzing the sympathetic innervation of the capillaries of the extremities by a constriction band applied for five minutes and measured the resultant effects by means of Pachon's oscillometer.

Direct measurement of skin temperature has been attempted, and recently Ipsen[6] published a considerable series of observations based on "skin-felt" temperatures, i.e., temperatures recorded with a mercury thermometer on areas of skin previously covered for a consid-

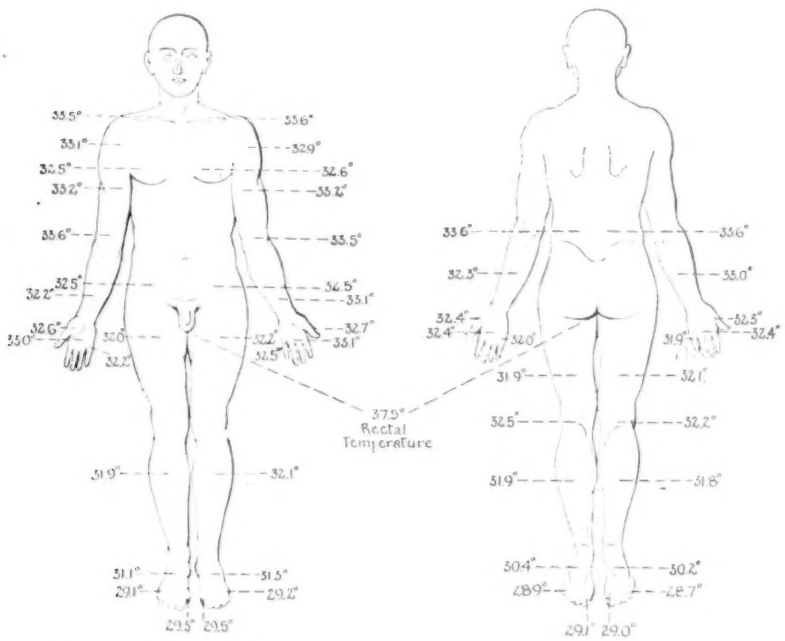

Fig. 1.—Average skin temperature of fifty normal medical students.

erable period of time by strips of felt to control the factors of heat radiation and insensible perspiration. Such a method is obviously time-consuming and does not permit virtually simultaneous observations of several areas.

Electrothermal devices have been developed and used by many investigators, notably by Benedict and his coworkers,[7, 8] but as used in the past the junctions of the thermopile have been introduced into the barrel of a hypodermic needle. Such an arrangement, while valuable for obtaining temperature readings on the subcutaneous tissues, in its practical application is so unpleasant to the patient that it is not feasible to attempt a large number of readings on a single patient or any large series of normal readings.

The latest apparatus introduced for use in the study of peripheral vascular diseases is the Dermatherm, an improved electrothermal instrument for measuring surface temperature developed by the Taylor Instrument Company of Rochester, New York, under the direction of Dr. W. J. Merle Scott[9] of Rochester. This instrument is described as a thermopile with its sensitivity increased by placing four couples in series. The galvanometer is calibrated directly in degrees Centigrade. The reading in degrees is added or subtracted from the reading of the constant temperature couple which is maintained within a thermos bottle. This gives the surface temperature.

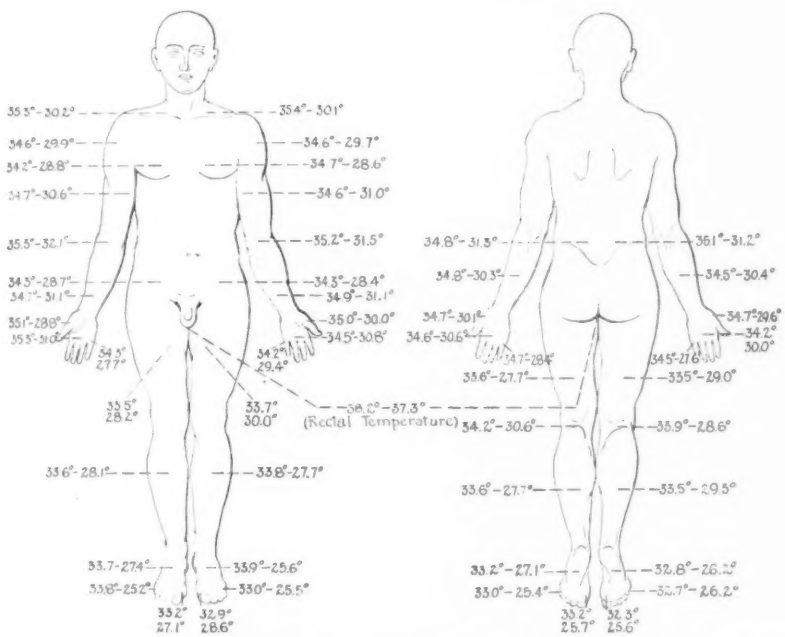

Fig. 2.—Maximum and minimum skin temperatures of fifty normal medical students.

This instrument has been used by Morton and Scott[10, 11] in studies of the vasoconstrictor gradient of the extremities. Studies have been attempted to show the influence of spinal anesthesia and inhalation anesthetics in the reduction of the vasomotor tone of the extremities.

White[12] has introduced procaine blockage of the peripheral sympathetics as a test to evaluate the factor of vasospasm in the extremities. He describes a simple technic for obliterating completely the vasomotor gradient of the extremities.

In this paper we shall present the results of studies with the Dermatherm on fifty normal medical students.

An attempt was made to set up a normal standard for the surface temperatures of the body in healthy young adults. For this purpose fifty medical students were chosen. The rectal temperature, pulse,

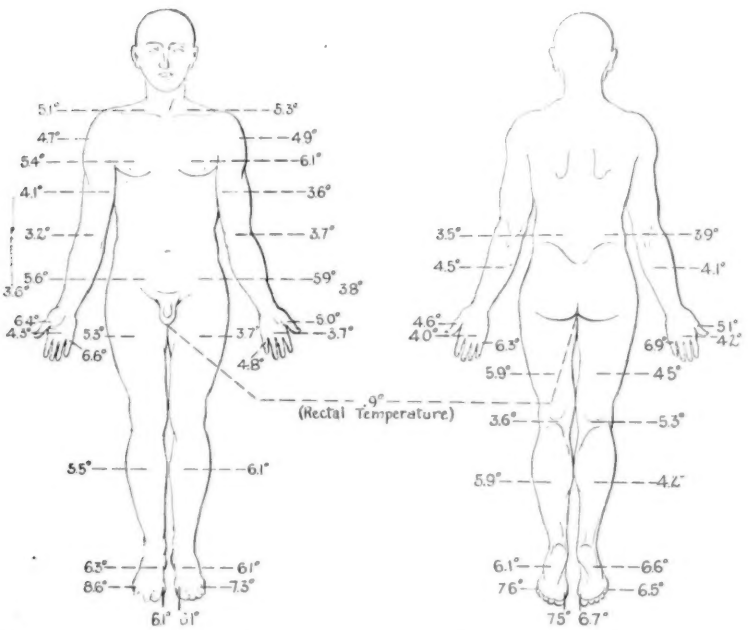

Fig. 3.—Variation of skin temperatures of fifty normal medical students.

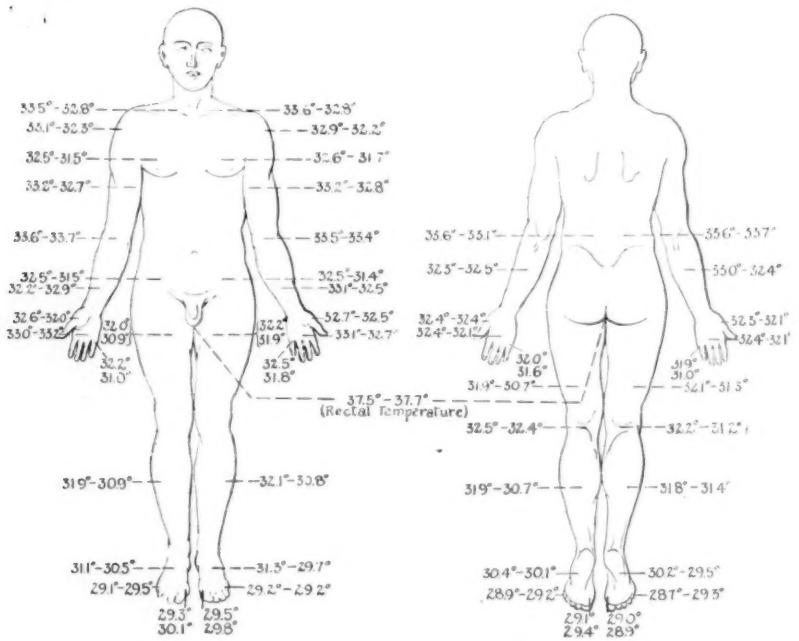

Fig. 4.—Average and mean skin temperatures of fifty normal medical students.

respiration, blood pressure, age, height, weight, and build of each student was recorded. Each student was then stripped in a room the temperature of which was 20° C., and after five to ten minutes the surface temperature was determined for fifty-two separate points over the body and extremities.

The technic of recording was quite simple. The thermo-couple was applied gently to a skin surface for from six to eight seconds, at the end of which time the galvanometer needle was at rest. A total of approximately fifteen minutes sufficed to record the pulse, respiration, blood pressure, rectal temperature and fifty-two surface temperature readings. The extreme ease with which these readings could be taken

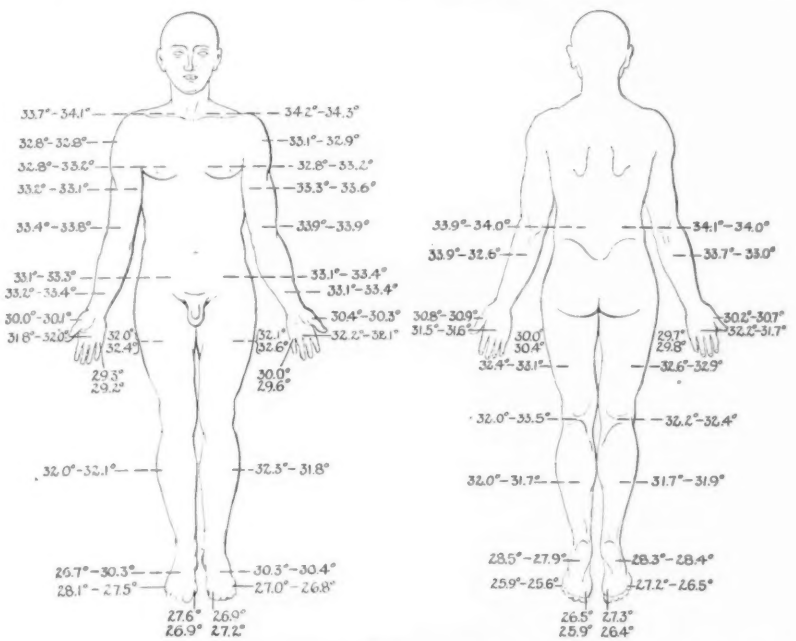

Fig. 5.—Effect of prolonged exposure of skin surface of five normal medical students to air at room temperature.

made possible the recording of a fairly complete series of skin temperatures on a large group of students. These results are presented in graphic form in Figs. 1, 2, 3, and 4.

DISCUSSION

An average of fifty determinations showed no difference between the two sides and no definite development of a vasomotor gradient in the upper extremities. In the lower extremities below the knee there was a definite development of a vasomotor gradient, the foot being one to two degrees below temperatures at the popliteal space. Temperatures at the base of the great and small toe were from two to three degrees below those in the popliteal space.

A considerable number of rather slender individuals were encountered with a moderate hypotension and a tendency to cyanosis in the extremities who showed a marked development of vasomotor gradient in the lower extremities and to a lesser extent in the upper extremities. It must be emphasized that in none of these individuals was there evidence of a pathological condition. They were merely individuals of the asthenic habitus. The extreme range in temperature variation was four to five degrees for the body, four to six degrees for the hands, and six to eight degrees for the feet. A comparison of the average and mean values tended to show that the most pronounced divergences from the normal were in the increased values found for the hands and the markedly decreased values found for the feet.

Stated simply, the "sports" were individuals with hot, moist, flushed hands and the individuals with cold, clammy, cyanotic feet.

Further study with the Dermatherm was undertaken to determine the effect when a longer period was allowed for the skin temperature to come to equilibrium with that of the air of the room. For this purpose a group of five medical students was tested as in the previous series. They then remained nude for one hour at room temperature (20° C.) and were again subjected to a complete series of skin temperature measurements. No really significant variations were observed after an exposure of one hour at a temperature of 20° C. These results are summarized in Fig. 5.

CONCLUSIONS

An attempt to establish normal skin temperature averages for a large number of definite points over the body and extremities by studies on fifty normal medical students with the Dermatherm (Tycos) resulted in the determination of an average value of 32.5° C. for the body after short exposure to the air with reduction of one to two degrees for the upper extremities and two to three degrees for the lower extremities. The vasomotor gradient is most pronounced in the hands and below the knees. The range of temperature variation of four to five degrees over the body, four to six degrees over the hands, and six to eight degrees over the feet suggests that no accurate average standard can be set up according to which all patients should be arbitrarily judged. The Dermatherm is, however, a compact instrument, simple and quick in its operation and apparently very accurate. Comparative studies on the same patient with the Dermatherm to determine the vasomotor gradient, occlusion index, etc., by use of various means of temporarily or permanently paralyzing the sympathetic supply to the peripheral vessels should prove of great value in estimating the relative part played by vaso-occlusion and vasospasm in the individual case of peripheral vascular disease.

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THE DURATION OF ELECTRICAL SYSTOLE AS AN INDEX OF MYOCARDIAL EFFICIENCY*

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BAZETT[1] noted that the studies of Patterson and Starling indicated a close relationship between the duration of systole and the degree of dilatation of the heart. Numerous physiologists have studied the relation of systole length, measured from mechanical or electrical records, to the heart rate, and several formulas have been evolved to express this relationship. This phase of the problem has been reviewed by Wiggers[2] and more recently by Cheer and Li,[3] who reported on the duration of electrical systole in 178 Chinese subjects. In a preliminary paper on patients with cardiac failure, Cheer[4] brings forward evidence which strongly supports Bazett's view that the duration of systole may be a reliable criterion of cardiac dilatation. In brief, the systolic index was definitely greater in the patients with cardiac failure than in the normal controls. The most extensive work on this problem is that of Fridericia,[5] who also observed a prolongation of systole in certain cases of cardiac failure.

In order to be of value to the clinician any index of cardiac efficiency must vary with the severity of physiological impairment and of symptomatic distress. It is also very desirable that there shall be but little overlapping of the range of indices of normal and of pathological conditions. Thus, the vital capacity is of value since very few normals have readings of less than 80 per cent and practically no bedridden cardiac patients have 60 per cent of the predicted vital capacity. In order to reexamine the value of the systolic index I have measured a relatively small series of tracings of three groups of cases: (1) clinic patients of various ages, with vital capacities over 80 per cent, normal electrocardiograms, and no demonstrable cardiac disease; (2) a similar group in which there was a left axis deviation in the electrocardiogram, but also without symptoms of cardiac failure (these patients were all ambulatory); (3) a group of patients with normal electrocardiograms or with left axis deviation, but with vital capacity less than 51 per cent of normal (these patients were all under treatment for cardiac failure). The series was small because it was immediately evident that while the average index was prolonged in cardiac disease, the normal and pathological indices overlapped in a considerable percentage of each group and that there was

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practically no difference between the group with left axis deviation without other evidence of heart disease and the group with advanced myocardial failure.

METHODS

The cases were taken in alphabetical order from the electrocardiographic files. The Q-T and R-R intervals were measured in the three standard leads, unless the T-wave was absent in one lead, as occasionally occurred. Two formulas were used to calculate the length of systole in terms of heart rate: $K = S / \sqrt{C}$, and $K = S / \sqrt[3]{C}$, where K is the systolic index, S the Q-T interval, and C, the R-R interval. A study of the indices in the 9 fastest, and 9 slowest normal men's hearts indicated that the $\sqrt{C}$ correction gave too high indices for the more rapid hearts. This probably explains, in part, the greater length of systole after exercise (noted by Bazett) and in women (Bazett; Cheer). However, the indices obtained in heart-block (5 cases) and in some normal patients with slow pulses suggested that below 60 per minute the $\sqrt[3]{C}$ correction gave too high an index. At 60 beats per minute the cycle length is 1 and the index is the same with either correction. It would, perhaps, be safer to use $\sqrt[3]{C}$ for cycles less than 1 and $\sqrt{C}$ for cycles longer than 1 second. I have used this method since it gives the narrowest range of variation in each of the groups measured by me.

RESULTS

(a) *Normal Men.* In 20 patients, ages twenty-three to sixty-six years, average age 41.3 years, the average systolic index when Q-T was divided by square root of R-R interval was 0.3841, if divided by cube root of R-R, 0.3722. For the nine fastest heart rates the square root formula gave an average index of 0.400, the nine slowest an average of 0.374. With the cube root formula the averages for the same groups were 0.376 and 0.374 respectively. The formula for systolic index adopted for use ($K = S \sqrt{C}$ when $C>1$, and $= S \sqrt[3]{C}$ when $C<1$) gave an average index (K) of 0.3714, maximum 0.401, minimum 0.347.

(b) *Normal Women.* The average age of 20 women was 34.6 years, the oldest was sixty, the youngest eighteen years. The square root formula gave an average of 0.3980, the cube root 0.3794; the final formula 0.3789, maximum 0.417, minimum 0.341. The average cycle length of the women was 0.751 sec., of the men 0.852 sec. The difference in systolic indices of male and female (0.0074) is only 2 per cent, and for this small series is not significant, particularly when the difference in cycle-length is considered. However, when 8 pairs of males and females having equal cycle length are compared, 6 women have larger indices, and only two men have indices greater than the corresponding female. On the average, the index of systolic duration of men is shorter, in this series of 8, by 0.011. I also paired 8 of Bazett's males and females, and here the same number, 6 females, had larger indices and the female average index was 0.030 larger than that of men with the same heart rates. It would seem, then, that independent of the average differences in heart rate, women have a duration of electrical systole 3 to 5 per cent greater than men.

TABLE I

	AVERAGE AGE	AVERAGE CYCLE LENGTH	AVERAGE VALUE OF $S/\sqrt{C}$	AVERAGE SYSTOLIC INDEX	LARGEST SYSTOLIC INDEX	PERCENTAGE OF GROUP LARGER THAN LARGEST NORMAL	PERCENTAGE OF GROUP LARGER THAN LARGEST OF LEFT AXIS DEVIATION GROUP
Normal Men	41.3	0.852	0.384	0.371	0.401	0	0
Men with Left Axis Deviation	53.6	1.050	0.408	0.404	0.441	60 per cent	0
Men with Cardiac Failure	62.5	0.751	0.403	0.402	0.466	40 per cent	10 per cent
Normal Women	34.6	0.751	0.398	0.379	0.417	0	0
Women with Left Axis Deviation	43.2	0.852	0.411	0.400	0.466	10 per cent	0
Women with Cardiac Failure	48.8	0.704	0.434	0.409	0.468	30 per cent	10 per cent

Systolic Index $= S\sqrt{C}$ when $C > 1$ and $S\sqrt[3]{C}$ when $C < 1$ second. The patients in the L.A.D. series were free from cardiac symptoms and had vital capacities over 80 per cent of the normal; those with failure had vital capacities 50 per cent or less.

(c) *The Duration of Systole in Abnormal Hearts.* The findings in 10 men and 10 women with left axis deviation but without heart failure and with vital capacity greater than 80 per cent, and in 10 men and 10 women with heart failure and vital capacity of less than 51 per cent (average 42 per cent) are summarized in Table I. None of these patients had any arrhythmia except occasional ectopic beats. Hypertension was present in about one-half of the first group. From the table it is evident that the systolic index is of little value in distinguishing the failing heart from the hypertrophied one, and that 65 per cent of failing hearts have indices within the normal range. Obviously the vital capacity is a more reliable and a much more sensitive index of cardiac function. The vital capacity of the group with heart failure was less than half that of the group with only left axis deviation; the systolic index was, on the average, the same, and only 10 per cent of the decompensated patients had indices greater than the largest index of the patients of the same sex who had cardiac hypertrophy without failure. It is, however, true that an index greater than 0.450 in men or 0.465 in women is rarely seen except in badly damaged hearts.

DISCUSSION

The results of my measurements of normal hearts show that, making due correction for the differences in cycle length, there still remains a real difference in the duration of systole in men and women, systole being longer in the latter. They also show that, both in men and in women, the shift in axis deviation to the left, occurring in middle age and particularly with a rising blood pressure, is associated with a prolongation of systole although not necessarily with any fall in vital capacity or symptoms of heart failure. Also, when heart failure does occur, the duration of systole is not increased beyond the normal range in about one-third of the cases, and the average duration is not much greater than in patients with hypertension and left axis deviation who have no cardiac distress or evidence of heart disease. The systolic index is therefore not of significance in distinguishing early cases of myocardial weakness, and a normal index does not rule out severe cardiac failure.

While the findings in this short series indicate that the duration of electrical systole cannot be correlated with the signs or symptoms of heart failure, they leave certain points open for further study. A very large number of normals, of various age groups and pulse rates, must be studied in order to define the limits of the normal, and to determine whether K should be based on the square root or the cube root of cycle length at various rates, or whether the cube root is also correct for rates slower than 60 per minute.

It has been held that the duration of mechanical systole is more sig-

nificant than the duration of electrical systole. From a small series of clinical records, in which sounds and electrocardiograms were recorded simultaneously, there was strong evidence against the superiority of mechanical systole, for in patients with gallop rhythm the electrical systole was from 8 to 25 per cent longer than the Q-A_2 interval. The systolic index, based on the Q-T interval, averaged 0.395, while that based on the Q-A_2 interval averaged 0.336 sec. In four normal subjects and four compensated cases of mitral stenosis, the Q-T and Q-A_2 intervals had the same average duration. This suggested that in myocardial failure, particularly in the hypertensive patients, mechanical systole may be shortened although electrical systole is prolonged. There is some experimental confirmation of this in the work of Wiggers and Katz,[6] who observed a shortening of mechanical systole on raising the diastolic pressure of dogs. However, they believed this to be evidence of good myocardial function.

It may be noted that my findings as to prolongation of systole in patients with left axis deviation confirm the observation of Meakins[7]; also there is fairly close agreement between the average normal figures, and the average figures in heart failure in this series and in Cheer's series of normals and his series of cases of hypertensive heart failure. Such agreement greatly increases the statistical significance of the findings in this short series.

CONCLUSION

The most satisfactory constant for the prediction of normal duration of systole at varying heart rates is obtained by the formula: $K = S / \sqrt{C}$ if C is greater than 1.0 second, and $S / \sqrt[3]{C}$ if C is less than 1.0 second. The cube root gives a more satisfactory constant, at rates between 60 and 120 per minute, than the square root of the cycle length.

There is a slight but definite difference in the duration of systole in normal men and women, even when individuals with the same heart rates are compared. Systole is 3 to 5 per cent longer in women.

In patients with heart failure the average index of duration of systole was 7 per cent greater than in normal individuals, and was the same as that of the group of patients with only left axis deviation. The average vital capacity of the first group was 94 per cent, of the left axis deviation group 86 per cent, of the heart failure group 42 per cent.

The systolic duration is not a satisfactory index of cardiac function, as only one-third of the failing hearts have systoles longer than the maximum found in a group of 20 normals of the same sex, and the duration is practically the same in hypertensive patients with left ventricular preponderance, but no evidence of failure, and in patients who are badly decompensated.

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ELECTROCARDIOGRAPHIC CHANGES IN PNEUMONIA*

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DAILY electrocardiographic records were taken on forty-five patients with lobar, and seven patients with bronchopneumonia. Our object was to learn whether any graphic evidence of cardiac involvement occurred during the disease. This is of importance for many reasons. Most clinicians feel that the circulatory apparatus plays an important rôle in pneumonia; in fact, failure of this system is believed to be a common cause of death. Pneumonia is cited as a cause of acute and chronic pericarditis, acute myocarditis and acute endocarditis. It may be an important factor in such cardiac disturbances as tachycardia, bradycardia, premature beats, auricular fibrillation, auricular flutter and heart-block.

No direct electrocardiographic study has hitherto been made in this disease. Robinson[1] in 1912 observed a prolongation of the P-R interval in the "dying heart" of two patients with pneumonia. Cohn and Jamieson[2] in 1917 in their investigation of the action of digitalis in pneumonia used fifty-six patients as controls, i.e., these patients received no digitalis. In two of these, P-R and T-wave changes were found; and in eight patients T-wave abnormalities were discovered. There is, however, no exact description of what these T-wave changes consisted. We, ourselves, have only considered T-wave inversions and flat T-waves. Again, Cohn and Jamieson usually took only one or two records in each patient throughout the entire illness, but it will be shown that the changes in pneumonia are often transient, and hence daily tracings are essential in investigations of this kind. In a more recent work of Burnett and Piltz[3] on the acute infections, T-wave, P-R and QRS changes were noted in six cases of pneumonia. Unfortunately these authors do not state whether their patients received digitalis. The effects of this drug must be excluded in order to be certain that the electrocardiographic changes are due to the disease itself. Two of us[4] have recently made a preliminary report on twenty-six pneumonia patients, but this larger series is reported in more detail. Electrocardiographic records were taken every day on patients who received no digitalis either before admission to the hospital or during their stay. It should be stated at the outset that the electrocardiographic changes reported in this paper, although at times of minor degree, were always definite. The changes were gradual, either in development or in disappearance, or in both, and hence it is felt that even the minor changes

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were of significance. They are not due merely to breathing, change of position, drugs, etc. Our tracings were always taken with the patient in the supine position.

The following three cases illustrate the chief electrocardiographic findings in our series.

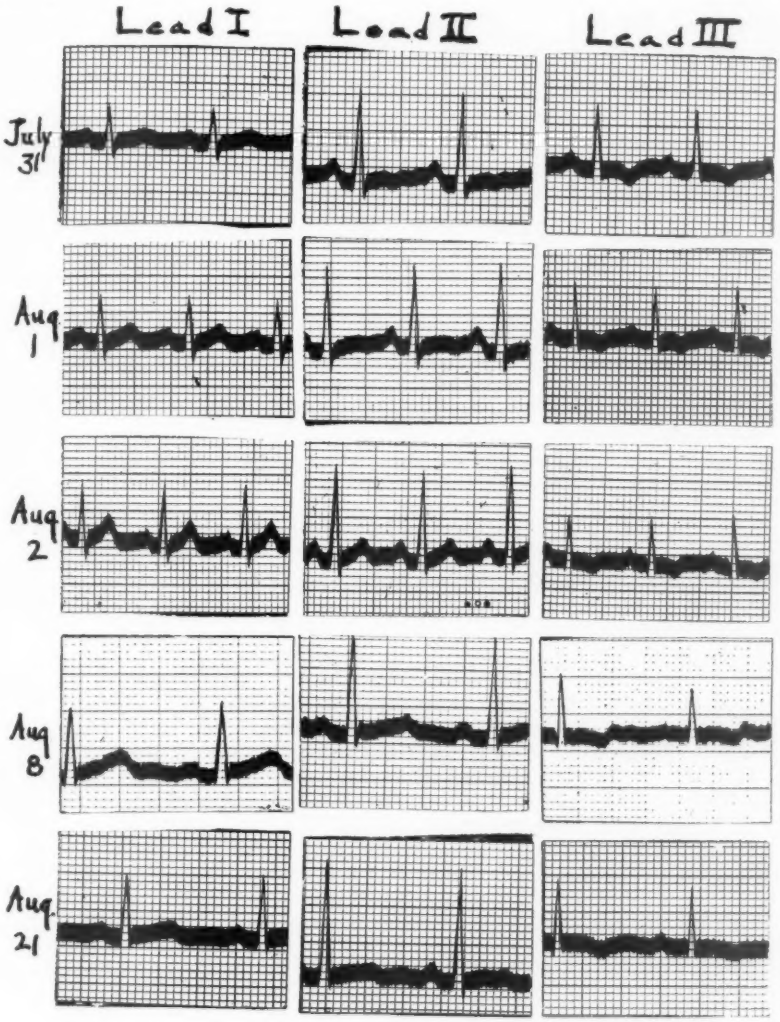

Fig. 1.—July 31, third day of illness. Temperature 103°-104.5° F., T_{2-3} inverted.
Aug. 1, temperature 103°-107° F., T_2 flat, T_3 inverted.
Aug. 2, temperature 100°-105° F., T_2 normal, R-T_{1-2} slightly abnormal.
Aug. 8, temperature normal, R-T_{1-2} above isoelectric level.
Aug. 21, return visit. R-T_{1-2} still above isoelectric level.

CASE 1.—Patient B. Mc. (316980), a girl of nineteen years, was admitted July 31, 1930, and discharged August 21, 1930. Four days prior to the hospital admission she had gone swimming and caught a "cold." Two days later a slight productive cough set in, followed by a chill. A sticking pain in the left chest then developed. On examination the patient was an acutely ill, well-developed and

well-nourished girl. Her temperature was 104° F., the pulse rate was 132 per minute, the respiration 28. In brief, signs of consolidation were found in the right upper lobe with involvement also of the right base. These findings were confirmed by the roentgen film. Examination of the heart revealed a marked tachycardia, but the heart sounds were good. A short systolic murmur was heard at the apex. No pericardial rub could be heard on admission or at any other time. On August 4, the heart sounds were slightly muffled. The temperature fell to normal on the fifth and sixth days by rapid lysis. Five of her many daily electrocardiograms are shown in Fig. 1. The inverted T-wave in Lead II, present on admission, disappeared within forty-eight hours. On the eighth of August, abnormalities of the R-T interval in Leads I and II were noted, occurring, interestingly enough, with the subsidence of fever. These R-T changes persisted throughout the stay in the hospital, and in fact were present a month later when the patient was examined at a follow-up clinic. At this visit she presented an overacting heart, and complained of some shortness of breath on exertion, easy fatiguability and palpitation of the heart. None of these symptoms had been present before her illness.

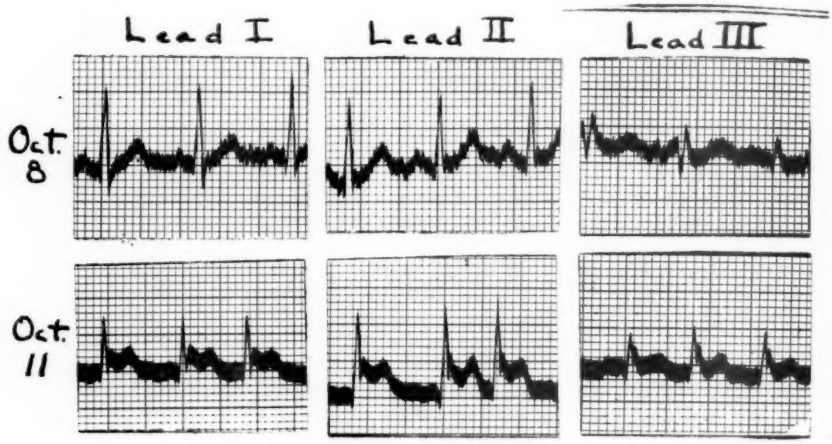

Fig. 2.—Oct. 8, sixth day of illness. Temperature 104° F., normal sinus rhythm. Oct. 11, date of death, temperature 101° F., auricular fibrillation, R-$T_{1\text{-}2\text{-}3}$ markedly abnormal.

Case 2.—Patient P. Z. (319101), a carpenter, fifty-eight years of age, entered the Mount Sinai Hospital October 7, 1930, and died October 11, 1930. His symptoms began four days before admission with a chill, and pain in the right side of the chest, which was aggravated by cough or by deep respiration. The patient was acutely ill and was very dyspneic. The signs of lobar pneumonia were present at the right base and were confirmed by teleroentgenogram. Pneumococcus Type I was found in the blood culture. The temperature ranged between 101° and 104° F. The heart rate was rapid, the heart sounds became poor and embryocardial in character. The dyspnea, orthopnea, and cyanosis increased. An oxygen tent was utilized to relieve the cyanosis. In Fig. 2 a normal record is seen. Three days later, the day on which death occurred, a high take-off of the R-T was observed, together with auricular fibrillation and a ventricular rate of 130 to 210 per minute. The oxygen therapy produced no change in this electrocardiogram. A post-mortem examination was obtained and there were found a lobar pneumonia of the right lung, an acute fibrinopurulent pleuritis of the right lung, an acute fibrinopurulent pericarditis, and some arteriosclerosis of the aortic cusp of the

mitral valve, aortic valve and the aorta. The coronary arteries were patent throughout. There were numerous small foci of parenchymatous degeneration of the muscle fibers.

CASE 3.—Patient D. S. (317351), an eighteen-year-old Porto Rican was admitted August 12, and discharged August 26, 1930. There was a history of cold in the head with running nose, sore throat and cough of two weeks' duration and a more recent story of fever with pain in the left chest aggravated by cough and breathing for four days. One day before admission he coughed blood-streaked sputum. He was an acutely ill boy, with a stiff neck and signs of pneumonia in the left lower lobe. His temperature on admission was 103° F. Gradually and somewhat irregularly the temperature became normal by August 19. The electrocardiograms (Fig. 3) show at first a tachycardia of 105-115 per minute, an auriculo-ventricular conduction time of 0.16 seconds and normal R-T intervals. The P-R interval slowly increased to 0.20 seconds on August 18, with a heart rate of 54 per minute;

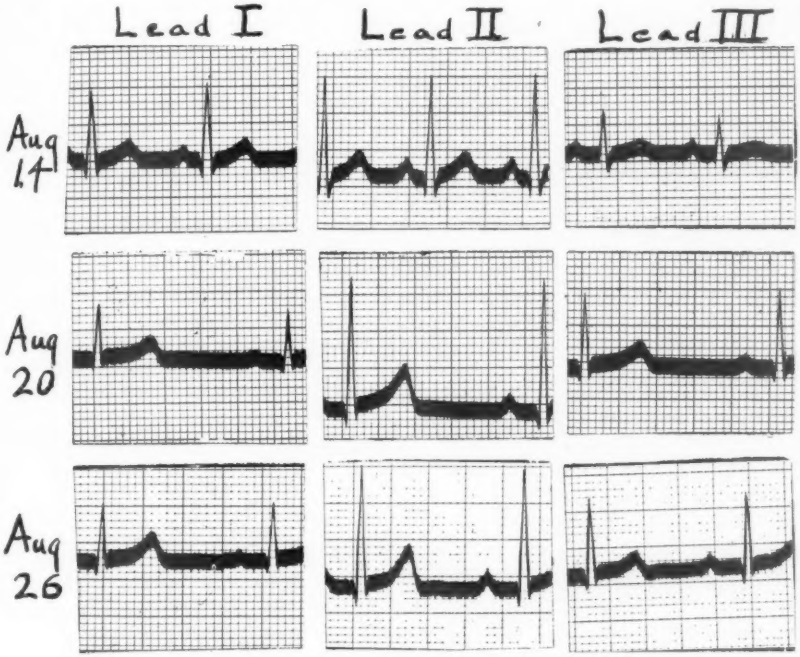

Fig. 3.—Aug. 14, sixth day of illness, temperature 98°-103° F., P-R 0.16 seconds.
Aug. 20, temperature normal, P-R 0.20 seconds, R-$T_{1\text{-}2\text{-}3}$ abnormal.
Aug. 26, temperature normal, P-R 0.22 seconds, R-$T_{1\text{-}2\text{-}3}$ abnormal.

then 0.22 second on August 25. On August 17, R-T abnormalities had become evident. This case illustrates the onset of partial auriculo-ventricular block, R-T disturbances and bradyeardia with subsidence of temperature to normal, i.e., with beginning convalescence of the patient. The P-R and R-T changes were still present on discharge.

Tables I and II summarize the electrocardiographic changes found in the series of 52 cases. The rate, rhythm, QRS group, auriculo-ventricular conduction time, T-wave, and QRS-T intervals, P-waves and ventricular preponderance were closely observed. The majority of our fifty-two patients were young adult males, only thirteen were females.

TABLE I

ELECTROCARDIOGRAPHIC CHANGES IN PNEUMONIA

	CASES	AVERAGE AGE	DEATHS	TACHYCARDIA	BRADYCARDIA	SINUS ARRHYTHMIA	LARGE-T	P-R INCREASE	INVERSION T_{1-2-3}	INVERSION T_{2-3}
Lobar	45	31	8	31	23	20	21	15	2	5
Broncho	7	39	1	4	1	2	0	3	1	2

	FLAT-T	INVERSION T_3 ONLY	R-T CHANGES	PREMATURE BEAT	AURICULAR FIBRILLATION	AURICULAR FLUTTER	ALTERNATION QRS	CHANGED PREPONDERANCE	CHANGE IN QRS	CHANGED P_3
Lobar	3	9	42 (93%)	1 Aur. 1 Vent.	2	1	1	2	3	2
Broncho	1	2	1 (14%)	1 Aur.	0	0	1	1	1	1

TABLE II

ELECTROCARDIOGRAPHIC CHANGES IN PNEUMONIA

	CASES	TACHYCARDIA	AVERAGE HIGHEST RATE	BRADYCARDIA	SINUS ARRHYTHMIA	LARGE-T	P-R INCREASE	INVERSION T_{1-2-3}
Living	43	26 (61%)	109 per minute	24	22	20	18	1
Dead	9	9 (100%)	159 per minute	0	0	1	0	2

	INVERSION T_{2-3}	TOTAL T INVERSIONS	FLAT-T	INVERTED OR FLAT-T	PREMATURE BEAT	AURICULAR FIBRILLATION	AURICULAR FLUTTER	ALTERNATION QRS
Living	5	6 (14%)	3	9 (21%)	2	0	1	1
Dead	2	4 (44%)	1	5 (56%)	1	2	0	1

An increase in the P-R interval, i.e., an increased auriculo-ventricular conduction time was a significant finding (Tables I and II) and occurred in 35 per cent of the cases. Although this delay was never so marked as one often finds in acute rheumatic fever, nevertheless it was definite. In thirteen patients the P-R interval increased to 0.20 seconds, in two patients to 0.21 seconds, in one patient to 0.22 seconds, and in two others there was a prolongation of the P-R interval to 0.24 seconds. The P-R interval increased as the patient became convalescent, in fact the highest figures were first noted on the day of discharge. No increase in the P-R interval was observed in any of the fatal cases. This is another way of stating that the delay in auriculo-ventricular conduction is a phenomenon of convalescence. Dykes[5] in 1912, by means of jugular vein and radial artery tracings, found a temporary partial heart-block in a twenty-three-year-old patient with a lobar pneumonia.

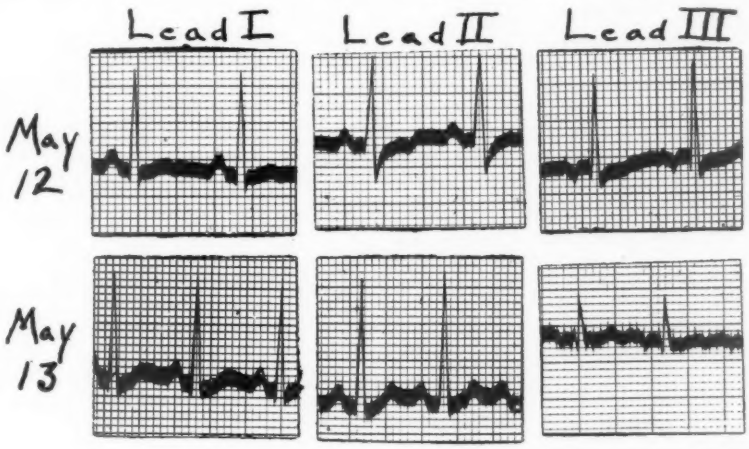

Fig. 4.—May 12, third day of illness. Temperature 100°-104° F., T_1 flat and slightly inverted, $T_{2\text{-}3}$ inverted, R-$T_{2\text{-}3}$ abnormal.
May 13, T-waves practically normal, R-T_2 still abnormal.

This occurred after the crisis and lasted for four weeks. In the illustration given by Cohn and Jamieson[2] at the end of their paper, an increase in the P-R interval to 0.21 seconds is present in a patient in the fourth week of convalescence. A delay in conduction occurring during convalescence, was reported by Hyman[6] in patients with influenza.

Ten patients were tested to study the effect of atropine sulphate on the auriculo-ventricular conduction time. In only two instances was there a definite decrease. In one individual a P-R of 0.20 seconds was reduced to 0.16-0.18 seconds, and in another to 0.16 seconds, on the administration of 1/50 grain of atropine sulphate intravenously.

For evidence of pericardial or myocardial impairment, close scrutiny was kept on the T-wave and RS-T intervals. Changes in each lead were followed daily. Negative T-waves in either Lead I or II were discovered in ten individuals. In three cases the inversion, or partial

inversion occurred in all three leads. Two of these patients died within two days after these changes appeared (Fig. 4). Negative T-waves in Leads I and II may be significant of an extremely toxic and fatal pneumonia. In seven patients the T-wave inversions were found in Leads II and III (Figs. 1 and 5). The mortality rate of 40 per cent in the ten patients with inverted T-waves is much higher than that of all the patients (17 per cent). Another way of emphasizing the significance of T-wave inversions is to state that of nine fatal cases the

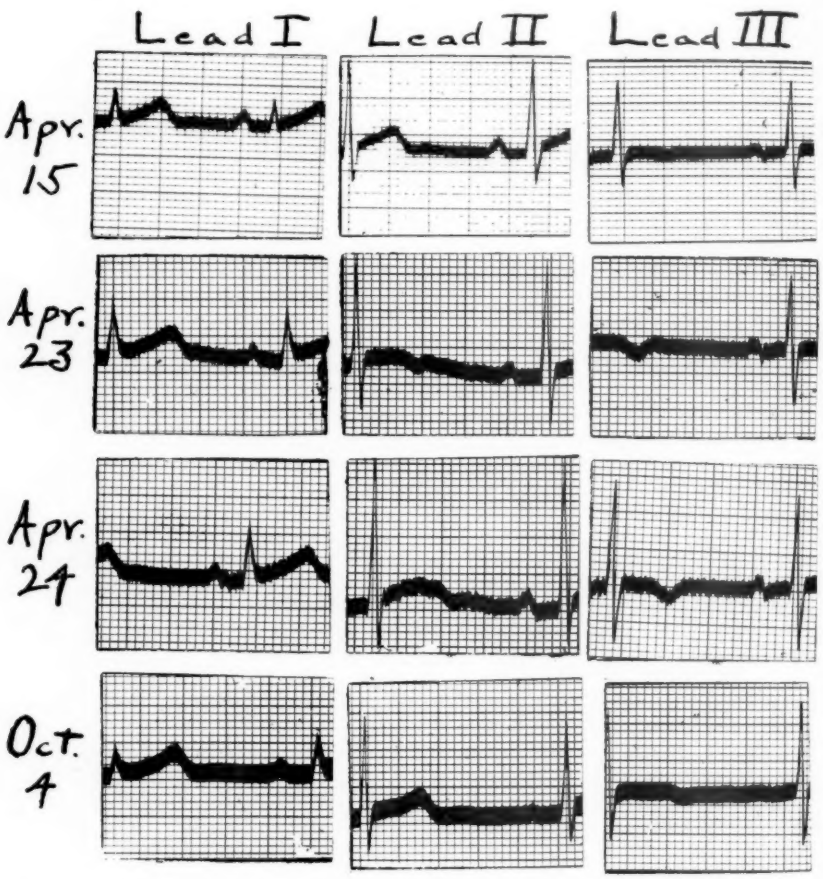

Fig. 5.—April 15, third day of illness. Temperature 100°-103° F., R-T_{1-2} abnormal.
April 23, temperature normal, T_{2-3} inverted. R-T_{1-2} abnormal.
April 24, temperature normal. T_2 normal. R-T_{1-2} abnormal.
Oct. 4, return visit. R-T_{1-2} still abnormal.

T-waves were inverted four times, or 44 per cent, whereas in those that survived the incidence was only 14 per cent (Table II).

Although the inverted T-waves were of the cove-plane shape, a contour described in coronary artery closure, no coronary artery involvement was found in any of the patients examined on the post-mortem table. Within 48 hours the inverted T-waves were normal again in all the patients who survived. In spite of their "coronary artery" con-

tour the T-wave inversions in pneumonia were always slight. They thus differed from the deep T-waves so often seen in coronary artery closure, rheumatic pericarditis, and hypertension.

Flat or iso-electric T-waves were noted in four individuals. One of these patients died. Actually flat T-waves were observed twelve times, but in eight cases these subsequently became inverted T-waves and hence these patients have been enumerated among those with T-wave inversions. However, these facts give additional significance to an isoelectric or flat T-wave since it may become inverted. Flat T-waves have been considered of significance in rheumatic fever, coronary artery disease, and pneumonia.[7]

The large number of RS-T changes were of interest and may be of importance (Tables I and II). These abnormalities, when marked, have been considered almost pathognomonic of acute coronary artery

Fig. 6.—Sept. 5, fifteenth day of illness. Alternation of the QRS group. Sept. 6, date of death.

closure,[8] and have been described also in acute rheumatic fever.[9] Levine[10] gave one illustration of R-T abnormalities in a patient with pneumonia, which occurred after return of temperature to normal. Shearer[11] reported a case with similar electrocardiographic findings, also present when the patient's temperature dropped to normal. Shearer's patient recovered, and no reason was found for the R-T change.

These abnormalities in the RS-T period were observed in forty-two of the forty-five patients with lobar pneumonia (93 per cent), but only once in the seven patients with bronchopneumonia (14 per cent) (Tables I and II, and Figs. 1, 2, 3, 4, 5). It should be said that in eleven cases these changes were slight. However, that they were definite changes is proved by the fact that either at the beginning or end of the illness, the RS-T intervals were normal. In other words, they were deviations from the normal for the particular patient. One of the most

striking examples of the RS-T changes was that of Case II, previously described, who was in the hospital three days with lobar pneumonia involving the entire right lung (Fig. 2).

Although Levine[10] believed that the R-T abnormality in pneumonia could be differentiated from that seen in acute coronary artery disease, it is our belief that this is impossible. However, in the former disease the R-T change returns to the base line whereas in acute coronary artery disease the T-wave becomes inverted. We have never seen this phenomenon in pneumonia.

The R-T deviations first occurred usually at about the fifth, sixth, seventh or eighth day of illness (Figs. 1 to 5). Actually they coincided with the drop of temperature and the beginning of convalescence of the patient. Usually they persisted throughout convalescence, and occasionally for weeks afterward (Figs. 1, 5). In all but four cases the R-T abnormalities were above the isoelectric level rather than below and in the great majority of cases occurred in Leads I and II only.

In thirty-five individuals a simple tachycardia was observed early in the disease, when the fever was high. The most marked tachycardia for the fatal cases averaged 159 per minute, whereas for those who recovered the average highest rate was 109 per minute. These numbers refer to the highest rates of the tachycardia noted in the patients, and not the average heart rate. The relation of tachycardia to prognosis has been noted and emphasized by clinicians for years. Osler[12] says, "Certainly the mortality increases very rapidly when the pulse rate passes 125."

A simple bradycardia was observed at some time or other in twenty-four patients. The slow rates occurred in convalescence and only when the temperature was normal. Rates as low as thirty-six beats per minute were observed. No slow rate was observed in the fatal cases. To ten patients $\frac{1}{75}$ to $\frac{1}{30}$ grain atropine was given intravenously. In seven individuals no response was obtained. One of these received $\frac{1}{30}$ grain when his rate was 120 per minute, and later during convalescence when his rate was 58 per minute. On the other hand three patients developed an increase in rate ranging from 20 to 75 additional beats per minute on administration of $\frac{1}{50}$ grain atropine sulphate.

A definite sinus arrhythmia occurred twenty-two times, usually during late convalescence, and usually when a bradycardia was present. Atropine sulphate did not alter the arrhythmia.

Change in size of the T-wave occurred in practically every patient with a bradycardia. As the heart rate became slower, the T-wave became larger. A difference of at least 2 mm. was noticed before such a change was accepted. This increase in size of T-waves was observed in twenty-one patients with lobar pneumonia and not once in bronchopneumoia.

Auricular premature beats were recorded twice and ventricular premature beats once. One of the patients showing auricular premature beats died. In one of the fatal cases an "alternation" of the QRS

complex was noted on the electrocardiographic tracing (Fig. 6) and this change was observed also in a patient who recovered. Auricular fibrillation was noted in two patients, both of whom died. Another patient who revealed an auricular flutter survived.

Changes in the P-waves and in the T-waves in Lead III were not uncommon, the former was found in three patients, the latter in eleven. A change to left axis deviation was observed three times. An alteration in the size of the QRS group was seen twice; a change from a widened QRS to one of normal dimensions, once; and a loss of notching and slurring, once.

There were nine fatal cases in this series of fifty-two patients. Postmortem examinations were obtained in all. One case (Case 2) has already been described and it was the only one in which the heart was severely damaged, as proved by gross and microscopic examination. In seven other cases the microscopic findings showed slight, moderate, or severe degrees of parenchymatous degeneration. The changes were enough to identify the hearts as damaged but not enough to have alone produced death. These eight patients all showed R-T changes. The ninth case, one of bronchopneumonia, had an entirely negative heart. In this patient no R-T changes were present.

In general, among the nine fatal cases, the tachycardia ranged from 105 to 210, with the average of 159, in contrast to the average highest rate of 109 among those who survived. Two patients had an auricular fibrillation; one an "alternation" of the QRS group.

In a comparison (Table II) of the fatal cases with those that survived, we at once see that a tachycardia occurred without exception in the former group and that the average of the highest rates was 159. Of those patients that lived tachycardia was present in 61 per cent. The changes so commonly observed during convalescence were absent or minimal in the fatal cases, i.e., the bradycardia, sinus arrhythmia, large T-waves and increased P-R intervals. The fatal cases showed T-wave inversions in 44 per cent; the living patients in only 14 per cent. Considering inverted and iso-electric (flat) T-waves together one finds a frequency of 21 per cent among those who survived as against a figure of 56 per cent among those who died.

The bronchopneumonia group (Table I) was distinguished by the low percentage of R-T changes, i.e., only 14 per cent, whereas in the lobar pneumonia cases the percentage was 93. To us this is the most outstanding difference, but its exact significance is not clear. Tachycardia, bradycardia, sinus arrhythmia and the development of large T-waves appeared to be less common in the cases of bronchopneumonia. We say this guardedly as the number of bronchopneumonia cases is small. The patients who survived revealed tachycardia only three times and the rate was never above 115 per minute. The fatal case showed a rate of only 130 per minute.

DISCUSSION

The occurrence of increased auriculo-ventricular conduction time late in pneumonia, independent of a bradycardia, deserves consideration. Clinicians usually interpret an increased P-R interval as indicating disease of the auriculo-ventricular conduction tissues. The increased P-R interval is very often seen in rheumatic fever, and occasionally in severe toxic disease. Its occurrence late in pneumonia, when the patient is up and about, calls for an explanation. It may be that the physical activity is too much of a demand upon the weakened heart, and results in an increased conduction time. Perhaps these patients were permitted out of bed too early. The electrocardiogram therefore may prove an important guide as to the time to discharge a pneumonia patient from the hospital, or when to consider him cured. Osler[13] pointed out that sudden death might occur when convalescence was well established. He said, "Collapse coming on a day or two after the crisis is much more grave, being usually an indication that the myocardium has sustained severe damage," and "Death may occur suddenly when convalescence is apparently well established."

The clinical implication of an abnormal R-T interval in pneumonia is not understood. In a patient with very marked changes of this sort who died an acute pericarditis and an acute myocarditis were present. On the other hand, there were at least nineteen patients with as marked R-T changes, as well as a large number with less marked R-T abnormalities, who recovered. The persistence of the R-T abnormalities throughout convalescence and even for weeks afterward may be of clinical significance. In eight patients in whom changes have persisted for weeks, there was a delayed recovery in the patient's strength, and dyspnea occurs on slight exertion. Complaints of palpitation, fatiguability, and even precordial pain, occurred long after convalescence. In two patients a second increase in the P-R interval occurred long after the auriculo-ventricular conduction time had returned to normal. In three patients a flat T-wave in Leads I or II became evident weeks after discharge from the hospital.

The significance of the electrocardiographic changes as a whole is an important one. We offer five possible explanations. The changes recorded on the graphic tracing may be a vagus nerve effect. The occurrence of a bradycardia, sinus arrhythmia, and an increased P-R interval during convalescence would lend plausibility to this theory. Atropine had some effect on the bradycardia, and auriculo-ventricular conduction time, but none on the R-T or T-wave changes. Even had the effect of this drug been more marked it still would not have proved much, for the vagus probably exerts its influence during pneumonia and during the convalescent period, just as it does in ordinary life.

It is well known that changes in position of the heart will produce changes in the electrocardiogram.[14] There is no definite proof that a

change in position or rotation of the heart occurs in pneumonia, although if Coryllos[15] be correct this condition occurs. His contention is that an atelectasis is present in the disease and that this draws the heart toward the affected side. In children there is good evidence that movement of the heart occurs in pneumonia.[16] However, before this question is settled, frequent roentgen films of the chest must be taken on pneumonia patients.

A third explanation comes to mind when one recalls the marked frequency of the R-T changes in the patients with lobar pneumonia, and the low incidence in bronchopneumonia. It may be that electrical conduction through massively involved lung is altered, whereas in the patchy involvement of bronchopneumonia, this does not occur. The altered electrical conduction in the lung may possibly produce the R-T changes.

Experiments have been performed in which the anoxemia, rather than an organic involvement of the heart and blood vessels, is said to play the important rôle in the disease. Animals with experimentally produced pneumonia often die of respiratory failure, the heart beating rhythmically for some time after.[17] Kountz and Gruber[18] produced anoxemia in animals and obtained high plateau R-T abnormalities. With a view of throwing some light on the question of anoxemia, an oxygen tent with 40 to 50 per cent oxygen saturation was used on six of our patients. Not the slightest alteration in the records was discovered. Additional evidence that the cause of the electrocardiographic changes is not an anoxemia is found in the fact that the RS-T changes persisted throughout convalescence and even after the patient's discharge from the hospital.

It is our impression that the electrocardiographic changes are caused by the toxic products of pneumonia on the heart muscle. This would apply to the T-wave changes, the R-T deviations, the impaired auriculoventricular conduction, bradycardia and sinus arrhythmia, but particularly to the first three of these. We feel that vagus nerve effect, displacement or rotation of the heart, altered conduction of the heart's electric current through inflamed lung, and anoxemia, are of minor importance and that an actual involvement of the heart muscle occurs. Post-mortem examination of eight of our nine fatal cases have all shown some degree of parenchymatous degeneration of the heart muscle; in one of these cases there was very marked involvement. In the ninth case there was no involvement. Moreover there may be physiological or chemical changes in the heart muscle which are not revealed by morphological study.

SUMMARY

Daily electrocardiograms were taken on forty-five patients with lobar pneumonia, and on seven patients with bronchopneumonia. The T-wave and R-T changes were very similar to those described in acute coronary

artery closure, and the P-R, R-T, and T-wave abnormalities similar to those observed in rheumatic fever. The electrocardiogram in these three diseases is therefore not specific.

In eighteen patients (35 per cent) there was a definite increase in the auriculo-ventricular conduction time, ranging from 0.20 seconds to 0.24 seconds. The impaired auriculo-ventricular conduction occurred when the temperature was normal and the patient was beginning to convalesce. Atropine sulphate affected the P-R interval only to a slight degree.

There were ten patients with inverted T-waves in Leads I or II and sixteen cases in all with either inverted or flat T-waves. These patients had a poor prognosis. The T-wave inversions occurred early in pneumonia when the prostration was marked. They showed a "cove-plane" or "coronary T-wave" contour, but were, however, always shallow and always transitory. No coronary artery involvement was found in the post-mortem examinations.

R-T abnormalities occurred in 93 per cent of the patients with lobar pneumonia. They first appeared with a fall of temperature to normal levels. The R-T deviations were similar to those observed in acute coronary artery closure but they never progressed to an inverted T-wave.

In only one case of bronchopneumonia were there R-T changes, in marked contrast to the frequency of such changes in the lobar pneumonia cases.

A tachycardia was present in thirty-five patients. The more marked the tachycardia, the worse the prognosis.

A simple bradycardia was found in twenty-four patients. The rate in these cases was often about 40 per minute, once it was as slow as 36 per minute. Atropine at times released the bradycardia.

Large T-waves were present twenty-one times, associated usually with the occurrence of a bradycardia.

A sinus arrhythmia was discovered in twenty-two individuals, and occurred in convalescence. It was sometimes present with the bradycardia, but often appeared later. Atropine had no effect on the sinus arrhythmia.

Premature beats occurred three times.

Auricular fibrillation was observed in two fatal cases.

"Alternation" of the QRS group occurred in two patients, one of whom died.

Auricular flutter was observed once. This patient survived.

Transient P-wave inversions in Lead III were recorded three times, transient T-wave inversions in Lead III alone, eleven times; a change in left axis deviation, three times; changes in the QRS group, four times.

The fatal cases showed marked tachycardia, a large number of T-wave inversions (44 per cent), and an absence of auriculo-ventricular con-

duction impairment, of bradycardia, of sinus arrhythmia, and of large T-waves.

It is suggested that T-wave, R-T, and P-R abnormalities are due to varying degrees of myocardial involvement and hence the electrocardiogram may perhaps serve as a guide as to when to permit a patient out of bed and when to consider him cured.

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Department of Clinical Reports

CYST OF THE PERICARDIUM*

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WASHINGTON, D. C.

SIMPLE cysts of the pericardium are practically unheard of. At least, I have been unable to find any reference in the literature to that lesion after a rather extensive search. Rarely one finds multiple cysts of the epicardium in association with chronic adhesive pericarditis or organized fibrinous pericarditis. Such a case was reported by Lauche.[1] Large cysts are found occasionally in primary sarcoma of the pericardium, as in the case of Perlstein.[3] Cysticerci and echinococcus cysts

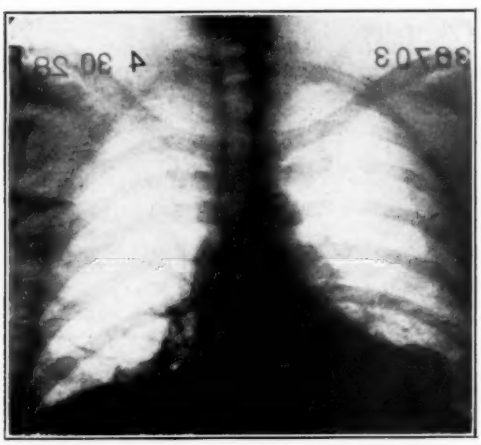

Fig. 1.—Roentgenogram of chest showing rounded lesion in region of apex of heart, which proved to be a simple multilocular cyst of the pericardium.

in the pericardial sac have been noted (Mönckeberg[2]). The following case is reported because of the rarity of the condition and because of the diagnostic difficulties.

CASE REPORT

The patient, a white man aged 52 years, began to have occasional attacks of mild epigastric pain in January, 1928. On April 10, 1928, while playing golf he experienced an acute attack of epigastric pain, followed by generalized abdominal soreness which finally localized in the epigastrium and right hypochondrium. The pain was constant with exacerbations, during which it radiated to the mediastinum, left shoulder and left side of neck. Physical examination on April 28 was negative

*From the Georgetown University School of Medicine and the Army Medical Museum.

except for the abdomen, which was distended and tender in the epigastrium and right hypochondrium. The heart was reported normal. Laboratory studies were negative except for the x-ray examination of the stomach and chest. There was an extensive filling defect of the stomach, most marked on the greater curvature, with retention of half of the barium meal after six hours and of one-fourth after 24 hours. Above the dome of the diaphragm and "partly overlapped by the shadow of the heart" there was a round shadow about 5 cm. in diameter (Fig. 1). The diagnosis was inoperable carcinoma of the stomach with metastasis in the left lung. The patient became progressively weaker, developed jaundice and died on May 28, 1928.

Necropsy had to be performed through an abdominal incision. There was a large ulcerating carcinoma on the greater curvature of the stomach about 3 cm. from the pylorus and several cm. in diameter, a typical adenocarcinoma microscopically. The liver weighed 3000 grams and was invaded by numerous large and small metastatic nodules. The lungs were normal. The heart was normal, but

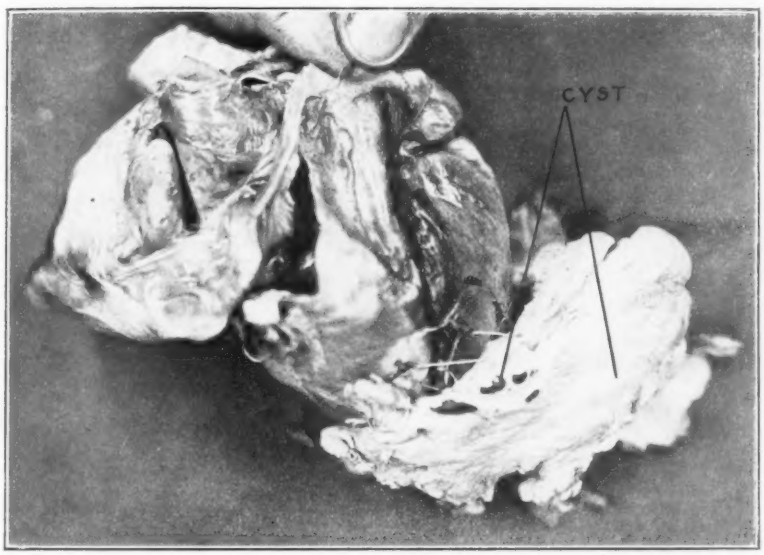

Fig. 2.—Cyst of the pericardium, reconstructed after dissection. The cyst is partially imbedded in the pericardial fat, so that its exact outline is not apparent, but the large white area indicated by the lines is the cyst.

projecting externally from the parietal pericardium at the apex and just above the diaphragm was a thin-walled, multilocular, ovoid cyst, 4.5 cm. long and 2.5 cm. thick, filled with clear, slightly yellowish, watery fluid (Fig. 2). The lining of the cyst was perfectly smooth, very thin, fibrous, and partially imbedded in the pericardial fat. It was intimately associated with the parietal pericardium and undoubtedly originated in it. There was no evidence of tumor in this region and no adhesive pericarditis. The cyst was probably derived from a lymphatic vessel of the parietal pericardium.

COMMENT

From the standpoint of roentgenographic diagnosis of the cyst one would have to decide first whether the shadow cast by it was that of a lesion in the lung or one associated with the heart. In this case it was

assumed to be in the lung because it fitted in well as a metastatic lesion from a carcinoma of the stomach. Under other circumstances a fluoroscopic study would have revealed the fact that the rounded shadow at the apex of the heart was attached to the heart. Then the diagnosis should have included the following possibilities: aneurysm of the heart, tumor of the heart or pericardium, loculated pericardial effusion, hydatid or other cyst. In this case aneurysm could probably have been ruled out because of the absence of evidence of cardiac disease which would antedate the formation of an aneurysm, and because there was no expansile pulsation, although the latter would not necessarily have been present. Tumor of the heart would have been more difficult to eliminate. In the absence, however, of disseminated metastases and because there was apparently only a single large lesion, secondary tumor of the heart could have been eliminated. Metastatic carcinoma of the heart occurs only as part of a more or less generalized carcinomatosis and is usually of the small shotty type of lesion. Elimination of this possibility would have been important had the patient's gastric lesion been discovered during the operable stage, since the interpretation of the lesion as a metastatic one might have discouraged surgical intervention.

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Department of Reviews and Abstracts

Selected Abstracts

Nuzum, Franklin R., and Elliot, Albert H.: An Analysis of 500 Instances of Arterial Hypertension. Am. J. M. Sc. **181**: 630, 1931.

Five hundred instances of arterial hypertension, the patients being forty-five years of age or older and having a systolic blood pressure about 150 mm. of mercury are analyzed. Seventy patients with chronic nephritis selected from the above are studied separately. Two hundred and fifty patients in the same age group with an average systolic pressure of 120 mm. of mercury and having only minor noninfectious ailments serve as controls.

Past infections occurred slightly more often in the hypertensive or nephritis groups than in the controls. Acute nephritis and scarlet fever occurred more frequently in the nephritis group than in the 430 remaining hypertensives or in the controls. The incidence of syphilis and typhoid fever was lower than usually reported in hypertension. The number of past infections per patient was nearly identical in each group. All focal infections found in the physical, roentgenographic or laboratory examinations were tabulated for each patient. Head foci were almost evenly distributed among the groups. Focal infection was not the deciding factor in the development of hypertension in these groups.

Obesity was encountered twice as often in the hypertensive patients as in the controls. The average weight for hypertensive group was 10.3 pounds greater than for the control group. Obesity is a contributory factor in the pathogenesis of hypertension. Familial tendency was less important in these series than in other reported studies. A positive history of familial vascular disease was obtained in about 30 per cent in both groups.

Palpable or ophthalmoscopic evidence of arteriosclerosis was found in 17.6 per cent of the main hypertensive group, in 24.2 per cent of the nephritic group and in 14.4 per cent of the control group. Arteriosclerosis of the larger vessels probably has little relation to hypertension.

Olcott, Charles T.: Rupture of a Coronary Artery, Hemopericardium. New Eng. J. Med. **204**: 760, 1931.

A case of a man of sixty years is presented with pericardial hemorrhage following rupture of the circumflex branch of the left coronary artery. There was an interval of fifteen hours between the admission symptom of precordial pain and death. Atheroma was considered the causative factor.

A review of the literature reveals thirty other cases of rupture of a coronary artery. The etiology of the rupture was not clear in ten cases; in fourteen there were atheromatous changes in the vessels, ten without aneurysm; in five there was an infectious embolism, four of whom had aneurysm; and luetic changes were present with aneurysm in two. There were nineteen males, eleven females and one not stated. The average age of the atheromatous patient was sixty-five; of the infectious 19.2 and of the luetic 46. Rupture occurred in the left artery eleven times; in the right eight times; in both three times and not stated in nine.

Bramwell, Crighton, and Ellis, Reginald: Some Observations on the Circulatory Mechanism in Marathon Runners. Quart. J. Med. 24: 329, 1931.

The observations on which this paper is based were made at the last Olympic Games at Amsterdam where the authors examined altogether more than 200 athletes including runners, weight lifters, swimmers, wrestlers and competitors in various other events. The article deals with the findings made by the authors on the cases studied as well as with a discussion of the various principles involved in exercise and the response of the heart to strain and training. It represents a brief well presented discussion of this very important subject and should be of interest to all. They noted that the individuals in the marathon races were inclined to be older, smaller and with a slower pulse rate and a slightly higher blood pressure. They believe that the marathon runner requires a greater stamina which may be found more frequently in older men rather than in younger athletes. They believe that the younger athlete is more inclined to run himself out and to use no caution in conserving his strength. The sprinter is of much less interest than the marathon runner to the cardiologist. His chance of success depends more on perfect neuromuscular coordination. He can run 100 meters without taking a single breath and can trust to the buffering mechanism in his blood and muscles to deal for the moment with all the lactic acid produced. So far as the immediate requirements of his muscles are concerned he might almost dispense with his heart.

For the longer distances on the other hand, the efficiency of the circulatory mechanism is all important; the long distance runner being dependent on the amount of oxygen he can obtain during the race.

The authors discuss all the oxygen requirements and glycogen balance found in athletes of this type. They point out the danger of glycogen death to be found in this group. Two men were on the verge of hypoglycemic convulsions. The use of sugar in the day previous to the race and possibly during the race is based on the utilization of glycogen.

It was found the heart was generally enlarged in marathon runners. The percentage of very large hearts being surprisingly high. They discuss the explanation of the difference that has been found by other workers in this same group. They believe that the recorded instances of small hearts found immediately after the race is due to the position of the diaphragm and to the change in position of the heart rather than to a change in actual size.

Cowan, John: Observations on Angina Pectoris. Brit. M. J. 1: 879, 1931.

The author describes various features of angina pectoris from observations on cases under his care. He notes the great variation in the severity of the pain in different patients and describes the site of pain as being generally behind the center of the sternum. The pain often is a feeling of impending dissolution. He notes that angina occurs more commonly in men than in women and most frequently in the fifth and sixth decade; the youngest paitent was twenty-three years old. He finds no special relationship between angina and the infections. Rheumatic fever was the most common antecedent in this series but its incidence was small. The association with syphilis is closer. Seventeen patients in the group studied had suffered from syphilis. He believes that muscular anoxemia accounts for the actual attack.

In this series a post-mortem examination was obtained in thirteen cases; of these twelve presented infarcts or fibrosis of the muscles, the coronary arteries being extensively diseased. In two cases there was rupture of the heart. Vasomotor disturbances not infrequently accompanied the attacks. The association between angina and the excessive use of tobacco is well established.

Treatment depends on the etiology in the particular case. In cases due to coronary disease every endeavor should be made to prevent undue strain on the heart until satisfactory anastomoses have had time to form and to supply the myocardium with sufficient blood. The treatment of a paroxysm is necessary but of less importance than its prevention. Angina is a danger signal, a sign of some harmful activity, and if we make the patient insensitive to his discomforts he will soon kill himself. For this reason surgical treatment while satisfactory to relieve pain should not be resorted to except in extreme cases.

McEachern, Donald, and Rake, Geoffrey: A Study of the Morbid Anatomy of **Hearts from Patients Dying with Hyperthyroidism.** Bull. Johns Hop. Hosp. **48:** 273, 1931.

This study has been made on all the cases of hyperthyroidism coming to autopsy in the Johns Hopkins Hospital since its opening in 1889. Thirty-seven cases were found in which there was conclusive evidence that hyperthyroidism existed. Ten cases were discarded because tissues or sections were not available. Twenty-five control cases were selected according to age for each of the six decades in which the cases of hyperthyroidism were scattered. These 150 cases were chosen consecutively from the autopsy records. Fourteen hearts of the total series showed no changes of the kind or degree not to be found in the control groups of similar age or which are not well recognized as occurring in general autopsy material in the absence of specific heart disease. In eight instances moderate perivascular or intermuscular fibrosis or small round cell infiltration was found. Similar changes were also encountered among the control cases though less frequently.

Conspicuous alterations were found in five instances; in three of which there was coexistent heart disease. Cardiac hypertrophy was noted in 16 of the 27 cases. No relationship could be established between the coincidence of auricular fibrillation or the duration of hyperthyroidism and the ultimate findings in the heart. Congestive heart failure occurred in five of the six cases that presented coexisting organic heart disease.

The authors believe that from this evidence it is impossible to ascribe the cardiac phenomena to structural changes in the muscle. It is pointed out that the heart from hyperthyroid animals continued to beat when isolated at a much faster rate than similar preparations from normal animals. Emphasis is placed on the desirability of studying the problem from the viewpoint of metabolic and functional alterations in the myocardium.

Carter, Edward P., and Baker, Benjamin M., Jr.: Certain Aspects of Syphilitic Cardiac Disease. Bull. Johns Hopkins Hosp. **48:** 315, 1931.

The authors have undertaken a study of the cases of syphilitic aortic disease, aortitis, aortic insufficiency either alone or combined with aneurysm and of aneurysm alone, admitted to the wards of the Johns Hopkins Hospital since 1910 at which time the Wassermann test came into accepted use. They have completed a detailed analysis of the first 100 cases. This has been supplemented by the pathological findings in those cases that came to autopsy. Their determinations are based chiefly on this series together with certain additional clinical material including statistical figures of the remaining cases of the entire series of 867. They have found the increased incidence of syphilis in colored patients, being about three times more frequent in colored males than in white males. They believe that every individual having a syphilitic infection is a potential subject of cardiovascular disease. What constitutes the predisposing factor which determines the peculiar arterial inversion with the ultimate involvement of the aortic ring or the development of an aneurysm is not clearly understood.

The question as to why the coronary artery escapes a similar fate has not been satisfactorily answered.

The Wassermann reaction was positive in an extremely high percentage of cases. Latent period from the day of the primary lesion to the first appearance of subjective symptoms was fifteen years and five months; two extremes being three years and thirty-nine years. Various symptoms are discussed. It was noted that auricular fibrillation was entirely absent in this series of 100 cases. Treatment of these patients is discussed and an extensive bibliography is included in the article.

Raab, W.: Central Vasomotor Irritability. Contribution to the Problem of Essential Hypertension. Arch. Int. Med. 47: 727, 1931.

In decerebrate cats with the vagi cut, the following experimental results were obtained:

1. There was a strong increase of the arterial blood pressure for a period up to two hours by the continuous perfusion of the brain stem with blood containing abnormally high amounts of lactic acid.

2. Hyperirritability of the vasomotor centers resulted under the influence of a shortage of oxygen or perfusion with lactic acid, or with the injection of lactic acid into the suboccipital cavity. The inhalation of carbon dioxide causes a considerably greater rise and the hyperventilation a greater fall in blood pressure under these conditions than occur under normal conditions.

3. Sensitive stimuli cause higher rises of blood pressure during the conditions mentioned than they do normally.

4. The effect of epinephrine is considerably weakened and inverted during the lack of oxygen; it is scarcely altered during perfusion with lactic acid.

5. Acetic acid increases the irritability of the vasomotor center in the same way as lactic acid; alkali gives irregular effects.

6. These experimental results correspond to the following characteristic features of essential hypertension: (1) High blood pressure; (2) hypersensitivity to the inhalation of carbon dioxide (abnormal increase of blood pressure) and to hyperventilation (abnormal fall of blood pressure); (3) hypersensitivity to peripheral sensitive stimuli; and (4) weakened or inverted effect of epinephrine.

7. The conclusion was reached that the symptoms of essential hypertension can be considered due to the local need of oxygen and the accumulation of lactic acid within the vasomotor centers of the brain stem as a consequence of local circulatory disturbances. The actual level of the blood pressure in hypertension would accordingly be composed of the sum of the stimulus through lactic acid plus the pathologically increased responses to the stimulus of the normal carbon dioxide tension of the blood and of different kinds of sensitive and emotional stimuli.

Ayman, David, and Pratt, Joseph H.: Nature of the Symptoms Associated with Essential Hypertension. Arch. Int. Med. 47: 675, 1931.

The possibility of a psychic origin for the early symptoms associated with essential hypertension was suggested by the clinical experiments of one of the authors. This idea was further encouraged by an earlier study in which 82 per cent of 40 hypertensive patients were definitely relieved of their symptoms by suggestion. Added support for this opinion was afforded by the widespread belief that as in psychoneuroses, the greater relief from the symptoms of which hypertensive patients complain may be obtained by the removal of worries, fears and other disturbances in the psychic sphere. The cause of this similarity, the problem of the relation of the symptoms presented by hypertensive patients to those observed in the psychoneuroses, seemed worthy of study.

This study has consisted of noting the symptoms associated with essential hypertension and those of the psychoneuroses. It was found that the early symptoms could not be differentiated between the two conditions either by their incidence or by their general and individual characteristics; that in both groups of patients no abnormality on physical or laboratory examination could be found adequate to explain the symptoms and finally that in both groups of patients a significant degree of maladjustment of emotional difficulties was found to explain the development of symptoms at the time they appeared. Additional evidence that the early symptoms associated with essential hypertension are due not to organic changes but to the emotional maladaptation of the patient can be noted in the results of treatment. While it seems reasonable to conclude that the early symptoms associated with essential hypertension are probably of psychic origin, the fundamental mechanism is not clear. Constitutional influences, endocrine products and possibly other factors may contribute to lessen the hypertensive patients psychic and physical capacity for withstanding the stress and strain of life.

Wishnofsky, Max, and Byron, Charles S.: Carbohydrate Metabolism in Hypertension. Arch. Int. Med. **47:** 790, 1931.

A dextrose tolerance test was performed on 10 patients suffering from hypertension. The blood sugar and the respiratory quotient curves were studied simultaneously. In six of the ten cases the blood sugar during fasting was higher than normal. It was shown that all patients with hypertension have high blood sugar curves. The respiratory quotient curves were normal in nine of the ten cases. This is adequate proof that there is no diminution in the secretion of insulin in hypertension and that these patients are neither potentially nor mildly diabetic. It disproves the theory that the disturbance in carbohydrate metabolism in hypertension is caused by sclerosis of the blood vessels of the pancreas. In the case in which the respiratory quotient curve was lower than normal diabetes mellitus independent of the hypertension could be considered to exist.

The theory that hyperadrenalemia is the cause of the disturbance cannot be proved in the present state of knowledge.

The mechanism concerned in producing this disturbance in carbohydrate metabolism is unknown and awaits further research for its elucidation.

Boswell, Clarence H., and Palmer, Harold D.: Progressive Thrombosis of the Pulmonary Artery. Arch. Int. Med. **47:** 799, 1931.

The authors report a case of a man aged thirty-nine years who had definite symptoms for some time prior to death which suddenly became aggravated and terminated fatally in a relatively short time. Post-mortem examination revealed thromboarteritis of the pulmonary artery with complete occlusion. The antemortem diagnosis had been myocardial injury. The thrombus at post-mortem seemed to be of some age, being well organized and in places canalized; though old, the thrombus became complete only during the last few hours as is shown positively by the newer portions of the thrombus. The thrombus on the left side was much less extensive and probably the result of right-sided retrogression. There was no evidence of chronic congestion showing that the heart was competent up to the time of the last sudden occlusion.

The authors suggest this to be a case of thromboarteritis in the pulmonary artery and not embolic. The sequence of events may have been: (1) acute respiratory infection occurring five weeks before death resulting in (2) lymphadenitis and bronchitis; this infection extended into the pulmonary artery as (3) an arteritis. The high coagulability of the venous blood in the pulmonary artery accompanying

the sepsis, together with a low blood pressure slowing the stream over a damaged artery lining, produced (4) a thrombus which was not extensive enough to cause death at that time. Later, after a good night's rest with slowing of the blood stream during sleep (5) another thrombus formed and the symptoms appeared with the activity on awakening. (6) Death did not occur until the new portion had retrogressed far enough to occlude the larger pulmonary branches.

Had this patient lived longer the complete syndrome on which the diagnosis of Ayerza's disease could be made might have developed; hypertrophy of the right side of the heart from the extra work thrown on it; polycythemia from the demand for more oxygen carriers; sclerosis of the pulmonary artery; chronic cough; cyanosis and later serious cardiac failure.

Sutton, Lucy Porter, and Wyckoff, John: Digitalis. Its Value in the Treatment of Children with Rheumatic Heart Disease. Am. J. Dis. Child. **41**: 801, 1931.

Twenty-five cases of digitalization in twenty-two patients with heart failure associated with active rheumatic heart disease under controlled conditions, digitalis of known biologic activity being used, are reported. In twenty-four digitalizations of twenty-one children, the average calculated dose necessary to produce the effect of digitalis was 0.15 cat units per pound of body weight. All of these patients showed some improvement in the signs of heart failure when fully digitalized. It was possible to produce the effect of digitalis without producing toxic symptoms in the majority of cases.

The authors conclude that digitalis is of value in the treatment of children with heart failure. It is effective in doses comparable to those required by adults without necessarily producing intoxication. It is effective in the presence of active infection of the heart.

Blackford, L. Minor, and Hoppe, Lewis D.: Functionally Two-Chambered Heart. Am. J. Dis. Child. **41**: 1111, 1931.

A case of an infant aged six and one-half months is reported with clinical, laboratory and post-mortem observations. The right atrium opened through the foramen primum into the left atrium which in turn opened through the mitral valve into a single ventricle. The tricuspid valve was absent. A small right ventricle in the mass of ventricular muscle between the stenosed opening in the interior wall of the large ventricle and a second stenosis at the beginning of the bulbus cordis was revealed on detailed dissection. The aortic valve was normal though the pulmonic valve was bicuspid. Extreme stenosis of the ventriculobulbar junction prevented the passage of an adequate amount of blood to the lungs. A theory is advanced to explain the changes in circulation that occurred in this patient.

Blumgart, Herrman L., Lawrence, John S., and Ernstene, A. Carlton: The Dynamics of the Circulation in Coarctation (Stenosis of the Isthmus) of the Aorta of the Adult Type. Arch. Int. Med. **47**: 806, 1931.

Coaretation of the aorta presents an opportunity to compare in the same person the dynamics of the circulation in arterial hypertension above the point of constriction with the dynamics of blood flow under lower pressure below the level of the stenosis. The results of an extensive study of two patients with coaretation of the aorta are presented.

The diagnosis of coaretation of the aorta was corroborated at necropsy in both patients.

The diagnosis was established in both patients by (1) arterial hypertension in the arms as contrasted with the relatively low blood pressure in the legs; (2) evidence of extensive collateral arterial circulation observed on physical examination and also made apparent by the erosions of the ribs seen in the roentgenograms of the chest; and (3) diminution and retardation of the arterial pulses in the legs.

Although arterial hypertension presumably had been present above the level of the coarctation in both patients for over forty years, physical examination and roentgenographic studies failed to disclose any perceptible difference in the degree of arteriosclerosis in the upper and lower parts of the body.

The arteriolar blood pressure in the arms was normal. This suggests that while increased peripheral resistance may, as in essential hypertension, be responsible for the arterial hypertension above the coarctation, this increased resistance is due not to increased arteriolar resistance but rather to the resistance offered by the constricted aorta and the collateral pathways.

The velocity of blood flow in the larger arteries of the leg was reduced and the arterial-arteriolar difference in blood pressure was greatly diminished. According to the measurements of oxygen in the blood, the blood supply to the tissues under resting conditions was nevertheless within the limits of normal.

The hypothesis that the small arterial-arteriolar difference in the local circulatory reserve is discussed. This condition is contrasted with that above the level of the coarctation where a marked difference in arterial-arteriolar pressure prevails.

Considerations are brought forward that suggest that symptoms of local circulatory insufficiency in the legs such as intermittent claudication and nocturnal cramps may be the earliest indication of a failing heart in patients with coarction of the aorta and should call for effective treatment, even before the appearance of dyspnea or any other evidence of circulatory stasis.

Morton, John J., and Scott, W. J. Merle: Methods for Estimating the Degree of Sympathetic Vasoconstriction in Peripheral Vascular Diseases. New Eng. J. Med. **204**: 955, 1931.

The authors have studied the surface temperature changes in suitable locations following the various types of anesthesia, both general anesthesia, spinal anesthesia and local anesthesia produced by anesthetizing peripheral nerves. They have studied both the methods of estimating surface temperature, the variations which may be found, and the errors which occur in these different types of anesthesia.

They believe that the number of degrees by which a given case fails to attain the lower limits of the normal vasodilatation level is of much more value in estimating the proportion of spasm and occlusion than the number of degrees through which the surface temperature rises. This is a point of particular importance in the management and prognosis of many of the cases of common vascular disease in the extremity.

Book Reviews

VERHANDLUNGEN DER DEUTSCHEN GESELLSCHAFT FÜR KREISLAUFFORSCHUNG. III Tagung. Theodor Steinkopff, Dresden and Leipzig, 1930. Pp. 150.

The papers and discussions collected here were presented at a meeting held in Dresden on June 11 and 12, 1930. The presentations are concise and the illustrations carefully prepared. The volume is of special value to those who wish to keep in touch with recent work in other countries and it is interesting to note the subject matter of the papers. There are papers on venous pressure and on changes in the peripheral circulation in hypertension, microphotographic studies of the capillaries, notes on respiration and chemical studies in relation to the circulation and respiration. The opening addresses are by Dr. Bürker (Giessen) on the red cells and by Dr. Lindhart (Copenhagen) on technical methods for the clinical study of problems of the circulation.

E. H.

DIE REFLEKTORISCHE SELBSTSTEUERUNG DES KREISLAUFES. By Dr. Eberhard Koch. Theodor Steinkopff, Dresden and Leipzig, 1931. Pp. 234 with 44 illustrations.

This is the first of a series of monographs entitled "Ergebnisse der Kreislaufforschung" edited by Bruno Kisch. It is devoted entirely to a consideration of the aortic (depressor) nerve (Coyn and Ludwig) and the sinus nerve (Hering and De Castro), and their receptors in the arch of the aorta and in the carotid sinus respectively. Because changes in heart rate and in peripheral vessel muscle tone are reflexly caused by changes of arterial pressure in the aorta and in the carotid sinus, Koch calls this mechanism "the pressor receptor mechanism of the circulation." Through this system the relative stability of blood pressure and heart rate is maintained. Neither the physical, chemical or hormonal changes in the blood, which undoubtedly play a part in the regulation of the circulation, nor the peripheral vasomotor mechanism are discussed.

In Part I the embryology, anatomy and comparative anatomy of this pressor receptor system are given and the literature is discussed. Of particular interest in this part is the description of the recent anatomical studies by De Castro on the sinus nerve and its receptors in the carotid sinus.

In Part II is found a complete résumé of the literature and a discussion of the normal and pathological physiology and the pharmacology of both the aortic depressor and the carotid sinus systems. It is based particularly upon studies of Hering, De Castro, and Heymans and some corroborative studies by the author. The importance of this section can be judged by the statement that a permanent denervation of the carotid sinus and the aorta will cause in experimental animals a permanent hypertension and that it is probably common in human beings to have an hypertension on such a basis. The effect of stimulation of the aortic and carotid sinus nerve on respiration, intestinal peristalsis, tonus of skeletal muscles and upon the function of organs of internal secretion is briefly discussed.

In Part III the author describes a method of changing and measuring the endo-arterial pressure in the carotid sinus. By this method he has been able to study quantitatively the reflex blood pressure and heart rate changes. The results of these experiments are fully discussed.

This monograph is a very well written and well illustrated work in which a newer and epoch-making concept of the physiology of the circulation is described. It is a treatise that should be read and studied not only by physiologists and anatomists, but since this newer physiology may change our present concept of diseases like hypertension, etc., it should be read and thoroughly digested by every practitioner in internal medicine.

C. S.

CLINICAL ELECTROCARDIOGRAPHY. By Sir Thomas Lewis. Ed. 5, London, Shaw and Sons, 1931.

The fifth edition brings this authoritative guide to the study of electrocardiography up to date without changing the character of the volume. It remains a small handbook of clinical electrocardiography, the result of years of experience compressed within 120 pages, and it needs no introduction to those who are familiar with the earlier editions or with the other writings of Sir Thomas Lewis.

E. H.

OCLUSION CORONARIA, BRUSCA Y LENTA. By T. Padilla and P. Cossio. El Ateneo, Buenos Aires, 1930.

In a richly illustrated volume of some 225 pages the Argentinian authors offer a clear and logical presentation of the subject of coronary occlusion. The first half of the book is devoted to a consideration of the anatomy and physiology of the heart and its circulation and of the pathological and etiological factors in coronary artery disease. In the second half the clinical aspects of coronary closure, both

sudden and gradual, are presented in a form which is simple and concise and yet is reasonably comprehensive. The numerous illustrations are clear and easily understood and contribute much to the value of the text. The bibliography is adequate and well chosen but is open to the criticism that frequently the same reference appears two or three times.

L. A. C.